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Synthesis and reactivity of gold thiolate cluster complexes

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SYNTHESIS AND REACTIVITY OF GOLD(I) THIOLATE CLUSTER COMPLEXES

By

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An Abstract of the Thesis Presented
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Chemical oxidation of dinuclear gold(I) thiolates of the formula $LLAu_2(SC_6H_4CH_3)_2$ [LL= dppp, bis(dipheny1phosphine)propane and dppb, bis(dipheny1phosphine)butane] and dinuclear gold(I) thiolate complexes with bridging a propane dithiolate ligand of the formula $LLAu_2(SC_3H_6S)$ [LL = dppp and dppb] was carried out using the mild oxidizing agent, ferrocenium, $[Cp_2Fe]PF_6$). Spectroscopic studies and elemental analysis showed the formation of gold(I) clusters, disulfide, and ferrocene as products of this oxidation reaction. The clusters, $[(dppp)AU_2(SC_6H_4CH_3)](PF_6)$ and $[(dppb)Au_2(SC_6H_4CH_3)](PF_6)$ were isolated after the chemical oxidation of $dpppAu_2(SC_6H_4CH_3)_2$ and $dpppAu_2(SC_6H_4CH_3)_2$, respectively. The clusters, [(dppp)2Au4(SC3H6S)](PF6)2 and [(dppb)2Au4(SC3H6S)](PF6)2 were isolated in the oxidation of [Au(dppp)(SC_3H_6S)Au] and [Au(dppb)(SC_3H_6S)Au], respectively.

Structures of the isolated clusters are proposed on the basis of 'H NMR, ^{31}P NMR, elemental analysis and by comparison to other clusters previously characterized in our lab.

Cyclic voltammetry studies of the four isolated clusters showed a peak at - 1.6 V vs. Ag/AgC1; however the starting gold(I) thiolate complexes showed two peaks at **–0.6** and 1.5 V vs. Ag/AgCl.

Thiolate-disulfide exchange reactions of the isolated clusters with $(SC_6H_4C1)_2$ were studied and compared with the starting gold(I) thiolate complexes. The gold cluster $[(Ph_3PAu)_4(SC_6H_4CH_3)_2](PF_6)_2$ was chosen for kinetic studies because it was well characterized and it was known to react with disulfide ($ClC_6H_4SSC_6H_4Cl$). Kinetic data was obtained by monitoring the reaction by 'H NMR. The plots of In [cluster] (M) versus time (s) show a linear relationship, which is consistent with first order in cluster concentration. The plots of In [disulfide] (M) versus time (s) show a linear relationship, which is consistent with first order in disulfide concentration. The data are consistent with the rate law:

$$\text{Rate} = k\,[(Ph_3PAu)_4(SC_6H_4CH_3)_2^{2+}][ClC_6H_4SSC_6H_4Cl]$$

The results showed that gold(I) clusters reacted faster than the neutral gold(I) thiolate complexes which suggest that Au ... Au interactions play a role in the disulfide exchange.

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CHAPTER 1

Introduction

History of Gold

Gold is a symbol of light and beauty for humans from early times. For millennia, humans of all cultures and civilizations have cherished the golden sun-like color, glitter and beauty. The symbol Au is not by chance the chemical symbol for gold, but it derives from the Latin word aurum meaning " shining dawn".

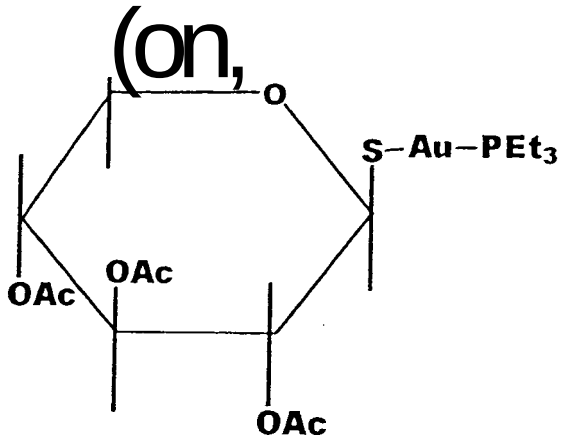
Historically, gold has been honored by many cultures. In ancient Egypt the golden sun-like color of gold was the symbol of the sungod, Horus. The ancient Egyptians probably developed the first systematic mining process for gold.' They not only created headdresses, jewelry and daily tools from this metal, but also placed gold in the pyramids with the dead to provide treasures for the afterlife. One of the most beautiful example is the mask of solid gold of Tutankhamun that was found over the head and shoulders of his mummy lying in a coffin of solid gold sheet, 2 mm thick, weighing over 90 kg. The treasure of Tutankhamun is proof that at least 3500 years ago the techniques of mining, refining, and working of gold had reached a very high level.[2a]

In addition to its historical and economic relevance, gold has a fascinating chemistry. Besides the many applications of gold to dentistry, monetary systems, jewelry and electronics, gold has been used in medicine throughout the history of civilization. The earliest medical use of gold can be traced back to the Chinese in 2500 BC. In

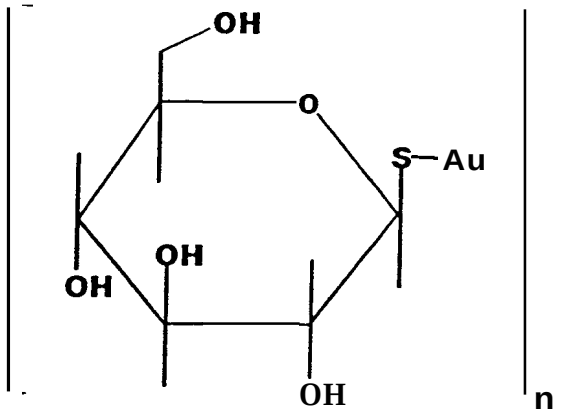
medieval Europe alchemists had a variety of recipes for an elixir known as aurum potable, which contained small amounts of gold. In the 17th century, a gold cordial was used for the treatment of ailments, such as fever, which were believed to be caused by a decrease in the vital spirits. A mixture of gold chloride and sodium chloride, $Na[AuCl_4]$ was used in the 19th century to treat syphilis.[3]

The modern use of gold complexes in medicine traces back to the experimental work of Robert Koch, who studied the bacteriostastic effect of $[Au(CN)_2]^-$.[4,5] In 1929, the French physician Jacques Forestier was one of the first to report the anti-arthritic activities of gold complexes.[4,5] In 1921, the Empire Rheumatism Council's double-blind multi-center trials demonstrated that gold drugs ware effective for many rheumatoid arthritis patients. The results showed that significant improvement was observed.[6] Gold(I) complexes have also been studied as potential anti-HIV agents and anti-tumor agents.[6,7]

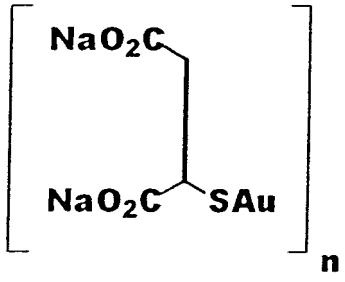
The early gold drugs used for the treatment of rheumatoid arthritis, for almost six decades, were water soluble gold(I) thiolate complexes, such as Solganol (gold(I) thioglucose) and Myocrisin (gold(I) sodium thiolate). In 1985, Auranofin was reported to be orally effective in human rheumatoid arthritis conditions.' Auranofin, $TATG(AuPEt_3)$, TATG = tetraacetylthioglucose, is a water-insoluble gold(I) phosphine complex. The structure of these compounds is shown in Figure **1.1.** The principal difference between Auranofin and the other drugs is the presence **of** the triethyl phosphine group bound to the gold atom. This would normally be expected to be toxic, but the phosphine liberated in the body is rapidly rendered harmless by oxidation.*The advantage of Auranofin over



Auranofin



Solganol



Myochrysine

Figure 1.1. Structure of gold(I) drugs used as anti-rheumatoid arthritis.

Solganol and Myochrysine is that it is administered orally rather than by injection and it appears to be less toxic.

Oxidation States of Gold

The reactivity of gold is also very interesting, and unique among the elements. In fact, elemental gold is stable and nonreactive to air at room temperature, and for this reason is often used as dental implants.[9a] The high melting point and ionization energy of gold seem to indicate that gold has "noble" or unreactive tendencies. The stability of gold is due in part to its extreme electrochemical potential, which is the lowest of any metal. Additionally, the electron configuration of gold ($[Xe]4f^{14}5d^{10}6s^{1}$) enhances stability. The filled ***d*** shells do not effectively shield the outer *s* electron from the nucleus. Therefore, the *6s* electron is attracted to the nucleus, and leads to high ionization energy, high melting point, and a smaller atomic radius. Gold can exist in a range of oxidation states from -I to +V.[2b] However gold +I and +III are the most common oxidation states and are most important in medicinal applications.[2b]

Gold(I) has a closed shell configuration ($[Xe]4f^{14}5d^{10}$). It forms two-, three- or four-coordinate complexes with appropriate choices of ligands. Two-coordinate gold(I) complexes are most favored and can be obtained primarily with soft ligands that are able to coordinate to soft metal centers. Among the soft ligands of biological interest are thiolates (such as cysteinate), thioethers and phosphines.[2b]

Closed-shell metal cations such as gold(I) would normally be expected to repel one another. Ions with closed shell configurations are generally unreactive. However the

presence of relativistic effects in gold changes the energy levels of the orbitals which leads to a certain degree of reactivity. In the case of gold, the *s* and p orbitals decrease in energy while the *d* orbitals increase slightly. Moreover, the energy of the *d* electrons is increased by spin – orbit coupling (i.e. interaction between the orbital angular momentum and spin angular momentum). As a result, the *s*, ***p***, and *d* valence electrons are much closer in energy. The *5d* (HOMO) and 6s (LUMO) gap is smaller when compared to systems in which there are no relativistic effects (see Figure **1.2).** This leads to s/p and s/d hybridization which enables gold(I) to form linear, 2- coordinate complexes.[9b]

Interestingly, gold complexes which may be formally regarded as containing gold(I) closed shell (d^{10}) cations, frequently show short Au...Au distances. By the end of the 1980s the term 'aurophilicity'was introduced in the literature.[9c]

In the solid state, evidence for a weak bond between gold atoms is provided by Au(I)-Au(I) separations (2.78-3.25 Å), which are less than van der Waals radii for gold.[9b] Schmidbaur et al. have estimated the strength of gold-gold interactions on the order of 5-15 Kcal/mol.[9d] The energies of gold(I)-gold(I) bonds are the same order of magnitude as those of hydrogen bonds.

Significance of Redox Chemistry to the Biological Chemistry of Gold

Previous studies have found that, gold(I) drugs, such as Auranofin and Solganol, can be oxidized to gold(III) and this may be responsible for some toxic effects in chrysotherapy (gold treatment).'[10-18] Chemical oxidation of Auranofin using hypochlorite

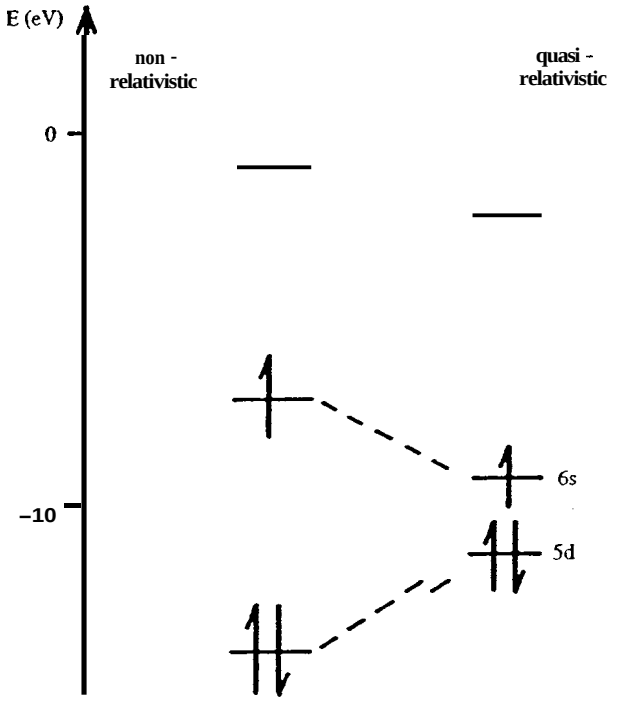


Figure 1.2. Non-relativistic and quasi-relativistic level of the gold(0) frontier orbitals.[9c]

showed that Au(III) can be formed in addition to a sulfonate from oxidation of the thiolate ligands.[19]

It has also been shown that several gold(I) drugs such as Auranofin, Solganol, and Myochrysine are capable of quenching $^1O_2$.[20] Singlet oxygen and other oxidizing species are produced in rheumatoid arthritis patients. Recently our group showed that Auranofin can be oxidized by using the mild oxidizing agent, $[Cp_2Fe]PF_6$, to form disulfide and a gold(I) cluster; however, Solganol is resistant to thiolate oxidation.[21]

Goals of This Study

Our group has been studying the structure and reaction of gold(I) phosphine thiolate complexes as models for Auranofin. The electronic structure of dinuclear gold(I) complexes, and their disulfide exchange reactions have also been studied by our group.[22,23,24] The electrochemistry of gold phosphine thiolates showed that a half-electron oxidation was found below 1.0 V for each gold center involved, and disulfides were found as one of the products.[25]

Our group recently reported that oxidation of a gold(I) phosphine thiolate complex results in the formation of a gold(I) cluster and disulfide.[22] For example, reaction of $Ph_3PAuSC_6H_4CH_3$ with the mild oxidizing agent, ferrocenium, proceeds according to Equation **1.1.**

$$2Ph_3PAuSC_6H_4CH_3 + [Cp_2Fe]PF_6 \longrightarrow$$

$$[(Ph_3PAu)_2\ (\mu\text{-}SC_6H_4CH_3)]PF_6 + 0.5\ CH_3C_6H_4SSC_6H_4CH_3 + Cp_2Fe \qquad \textbf{1.1}$$

This is interesting for two reasons. First, the oxidation chemistry of gold(I) thiolate complexes is potentially significant for the biological chemistry of gold drugs. Second, it represents an additional method for the synthesis of gold cluster.

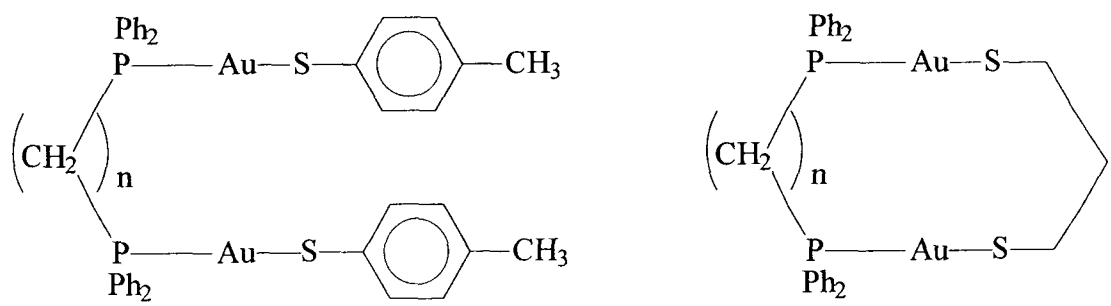
Gold clusters are typically made by reduction of suitable gold(I) precursors using suitable reducing agent such as sodium borohydride ($NaBH_4$).[26,27] Another procedure involves evaporation of gold atoms into hydrocarbon solutions containing phosphine ligands.[26,27] Changing the nuclearity of gold clusters through electrochemical reactions has been found to be an efficient procedure in preparation of gold clusters such as the tricationic cluster $[Au_9(PPh_3)]^{3+}$.[27] The most common procedure in preparation of gold clusters is the use of gold(I) transfer agents (e.g. R_3PAu^+ or the gold oxonium salt).[28]

Our group has also been studying the reaction of gold(I) phosphine thiolate complexes with disulfide.[24,29,30] These studies suggested that Au- Au interactions may play a role in activating the complex toward reaction with disulfide. For example, the mononuclear complex, $Ph_3PAuSC_6H_4CH_3$, reacts very slowly with disulfide according to Equation **1.2.**

$$Ph_3PAuSC_6H_4CH_3 + ClC_6H_4SSC_6H_4Cl \longrightarrow Ph_3PAuSC_6H_4Cl + CH_3C_6H_4SSC_6H_4Cl \qquad \textbf{1.2}$$

However, the dinuclear gold(I) complex, $dppmAu_2(SC_6H_4CH_3)_2$ which contains a Au-Au interaction in solution, reacts more quickly.[31]

There are two main goals of my mastere's thesis project. The first one is to extend the study of the oxidation of gold(I) phosphine thiolate complexes to include more examples of dinuclear gold complexes. These complexes, shown in Figure **1.3** were synthesized and thoroughly characterized previously by our research group.[31,32] Oxidation will be carried out by using the mild one electron oxidizing agent $[Cp_2Fe]PF_6$. Products will be characterized by ^1H and $^{31}P\{^1H\}$ NMR, elemental analysis, X-ray (where possible), and electrochemistry. These studies are reported in Chapter **2** of this thesis.



n = 3, $dppp(Au\text{-}p\text{-}tc)_2$
n = 4, $dppb(Au\text{-}p\text{-}tc)_2$

n = 3, $dppp(Au)_2(pdt)$
n = 4, $dppb(Au)_2(pdt)$

Figure 1.3. Structures of gold(I) thiolates studied in this thesis.

Where dppp = bis(diphenylphosphine)propane, dppb = bis(diphenylphosphine)butane, ***p***-tc = *p*-thiocresolate, and pdt = propane dithiolate.

The second goal of my master's thesis project is to study the reaction of gold(I) clusters with the disulfide, $(SC_6H_4Cl)_2$. The purpose of these studies is to determine whether clusters with **4** Au-Au interactions will react rapidly with disulfide in comparison to mononuclear and dinuclear gold(I) complexes that were studied previously in our group.[24,29,30] Specifically, my goals were to determine the rate law for the reaction of disulfide $(ClC_6H_4SSC_6H_4Cl)$ with one of the cluster complexes. This involved determining the order of reaction in cluster concentration and disulfide concentration, and calculating the rate constant for the reaction. Comparative kinetic studies were also done to determine the rates for other clusters, a mononuclear complex and several dinuclear complexes. These results are presented and discussed in Chapter **3** of this thesis.

References

1. Morrell, W.P. *The Gold Rushes;* Macmillan: New York, 1941.

2. (a) Morteani, G. in *Gold: Progress in Chemistry, Biochemistry, and Technology.* Schmidbaur, H., Ed., John Wiley & Sons, 1999, p 41. (b) Shaw, C. F., III in *Gold: Progress in Chemistry, Biochemistry, and Technology.* Schmidbaur, H. Ed., John Wiley & Sons, 1999, 260.

3. Fricker, S. P. *Gold Bull.*, **1996**, *29*, 53-60.

4. Higby, ***G.*** J. *Gold Bull.*, 1982, 25, 130-140.

5. Kean, W. F.; Lock, C. J. L.; Howard-lock, H. *Inflammo Pharmacology*, 1991, 2, 103-114.

6. Tepperman, K.; Elder, R. *Metal-Based Drugs*, 1994, *1*, 433-444.

7. Sadler, P. J.; Nasr, M.; Narayanan, V. L. in *Platinum Coordination Complexes in Cancer Chemotherapy,* Hacker, M. P.; Douple, E. B.; krakoff,I. H. Ed., Martinus Nijhoff, Boston, 1984, p 290.

8. Parish, R. V. *Interdisciplinary Science Reviews,* 1992, 17, 221.

9. Marx, J. *The Magic of Gold*; Doubleday and Company, Inc.: Garden City, ***NY,*** 1978. (b) Pyykko, P.; Declaus, P. J., *Acc. Chem. Res.*, 1979, 22, 276. (c) Klapotke, T. M. in *Organic Derivatives of Gold and Silver,* Patai, **S.** and Rappoport, Z. Eds., John Wiley & Sons, England, 1999,401. (d) Schmidbaur, H. *Gold Bull.* **1990**, *23*, 11.

10. Sadler, P. J., *J. Inorg. Biochem.*, **1995,** *54*, 225-228.

11. Isab, A. A.; Sadler, P. J. *Biochim. Biophys. Acta*, 1977,492, 322-330.

12. Shaw, C. F., 111; Cancro, M. P.; Witkiewicz, P. L.; Eldridge, P. L. *Inorg. Chem.,* 1980, *19*, 3198-3201.

13. Witkiewicz, P. L.; Shaw, C. F., 111, *J. Chem. Soc. Chem. Commun.,* 1981, 1111-1114.

14. Sadler, P. J. *Struct. Bonding,* **1967**, *29*, 171-219.

15. Shaw, C. F., III *Inorg. Prosp. Biol. Med.*, **1979**, *2*, 278-355.

16. Brown, D. H.; Smith, W. E. *Chem. Soc. Rev.,* **1980**, *9*, 217-239.

17. Takahashi, K.; Griem, P.; Goneaiez, J.; Gleichmann, E. *Metal-Based Drugs,* **1994,** *I* , **483.**

18. Schuhmann, D.; Kubicha-Muranyi, M.; Mirtcheva, J.; Gunther, J.; Kind, P.; Gleichmann, E. *J. Immunol.,* **1990, 145,213**

19. Shaw III, C. F.; Schraa, **S.;** Gleichmann, E.; Grover, Y. P.; Dunemann, L.; Jagarlamudi, **A.** *Metal-Based Drugs,* **1994,** *I* , **351-362.**

20. Corey, E. J.; Mehrotra, M. M.; Khan, **A.** U., *Science,* **1987,236, 68-69.**

21. Mohamed, **A. A.;** Bruce, **A.** E.; Bruce, M. R. M. unpublished results.

22. Chen, J.; Jiang, T.; Wei, G.; Mohamed, **A. A.;** Homrighausen, **C.;** Bauer, J. **A.,** Bruce, **A.** E.; Bruce, M. R. M. *J. Am. Chem. Soc.* **1999,121,9225-9226.**

23. Foley, J. B.; Gay, **S.** E.; Tunnel, C.; Wei, C.; Wei, G.; Jiang, T.; Narayanaswamy, R.; Foxman, B. M.; Vela, M. J.; Bruce, **A.** E.; Bruce, M. R. M. *Metal-Based Drugs,* **1999, 6,255.**

24. Dilorenzo, M.; Ganesh, **S.;** Tadayon, L.; Bruce, M. R. M.; Bruce, **A.** E *Metal-Based Drugs,* 1999, *6*, 247.

25. (a) Mohamed, **A. A.;** Bruce, **A.** E.; Bruce, M. R. M. in *Organic Derivatives of Gold and Silver,* Patai, **S.** and Rappoport, Z. Eds., John Wiley & Sons, England, **1999,** 313-**352.** (b) Jiang, T.; Wei, G.; Tunnel, C.; Bruce, **A.** E.; Bruce, M. R. M. *Metal-Based Drugs,* **1994,** *I* , **426.** (c) Mohamed, **A. A.;** Bruce, **A.** E.; Bruce, M. R. M. *Metal-Based Drugs,* **1999**, *6*, 233-238.

26. Van der velden, J. W. **A.;** Bour, J. J. ; Vollenbroek, F. **A.** ; Beurskens, P. T. ; Smits, J. M. M. *J. Chem. Soc., Chem. Commun.,* **1979,1162.**

27. Van der velden, J. W. **A.;** Beurskens, P. T.; Bour, J. J.; Bosman, W. P.; Noordik, J. H.; Kolenbrander, M.; Buskes, J. **A.** K. M. *Inorg. Chem.,* **1984,** *23*, **142.**

28. Lopez-de-Luzuriaga, J; Sladek, **A;** Schneider, W.; Schmidbaur, H. *Chem. Ber.* **1997,130,641.**

29. Dilorenzo, M. Master Thesis. University of Maine, **1997.**

30. Ganesh, **S.** Master Thesis. University of Maine, **1995.**

31. Narayanswamy, R.; Young, M. **A.;** Parkhurst, E.; Ouellette, M.; Kerr, M. E.; Ho, D. M.; Elder, R. **C.;** Bruce, **A.** E.; Bruce, M. R. M. *Inorg. Chem.*, **1993**, *32*, 2506.

32. (a) Jones, W. B.; Yuan, J.; Narayanaswamy, R.; Young, M. **A.;** Elder, R. C.; Bruce, **A.** E.; Bruce M. R. M. *Inorg. Chern.*, **1995,** *34,* **1996.** (b) Foley, J. B.; Bruce, **A.** E.; Bruce, M. R. M. *J. Am. Chem. Soc.*, **1995,** *117,* **9596.** (c) Schwerdtfeger, P.; Bruce, **A.** E.; Bruce, M. R. M. *J. Am. Chem. Soc.*, **1998, 220, 6587.**

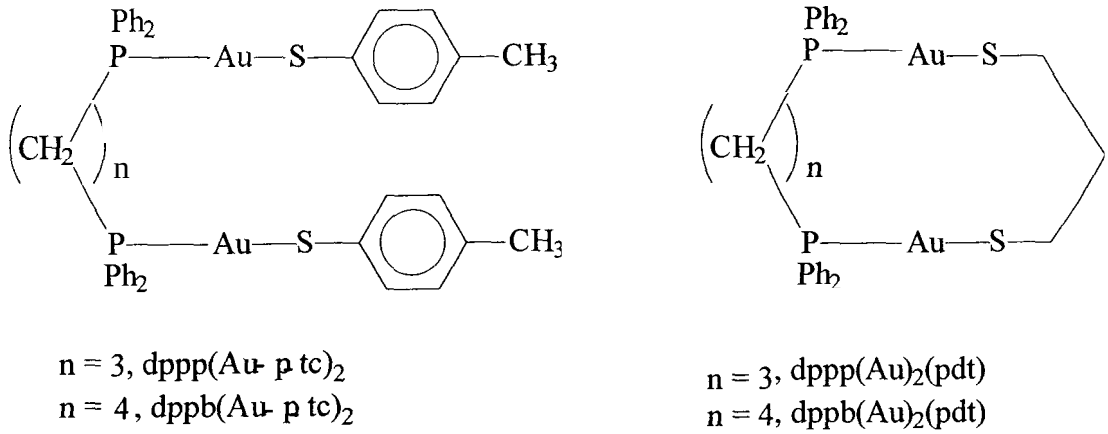
CHAPTER 2

Chemical and Electrochemical Oxidation of Phosphine Gold(I) Thiolate Complexes

Introduction

The biological activity of gold-sulfur complexes is well established and has led to the development of highly effective antiarthritis drugs, as well as complexes that show antitumor activity and inhibition of the HIV virus.' Our group has been studying the chemical and electrochemical oxidation of monophosphine gold(I) thiolates such as Auranofin and $PPh_3Au(SC_6H_4CH_3)$, as well as dinuclear phosphine gold(I) thiolates such as $LLAu_2(SC_6H_4CH_3)_2$ and $LLAu_2(SCH_2CH_2CH_2S)$ where, LL = a bisphosphine ligand.[2] These complexes are related to the antiarthritis drug, Auranofin, which contains gold(I) coordinated to phosphine and thiolate ligands (Figure **1.1).** Gold(I) clusters and disulfide were obtained in the chemical oxidation reactions of mono and dinuclear gold thiolates.[2] The products have been characterized by ^1H NMR, ^{31}P NMR, elemental analysis, and X-ray crystallography. For example, the X-ray crystal structure of the product obtained by oxidation of $Ph_3PAu(SC_6H_4CH_3)$ showed a cluster consisting of two monocationic $[(AuPPh_3)_2(\mu\text{-}SC_6H_4CH_3)]^+$ units dimerized to form a tetranuclear cluster? Chemical oxidation of $dppmAu_2(SC_6H_4CH_3)_2$, dppm = bis(diphenylphosphine)methane, formed an unusual cluster containing nine gold(I) atoms.[3]

A number of gold(I) phosphine thiolate complexes have been synthesized (Figure **2.1)** and characterized by previous students in our research group.[4] We wished to determine whether the previous oxidation reactions studied by Chen et. al could be generalized. Specifically, my goal was to study the oxidation of the four complexes shown in Figure **2.1.** Reaction products were characterized by using NMR spectroscopy, elemental ananlysis, X-ray crystallography, and electrochemistry, as appropriate.



n = 3, dppp(Au- p tc)$_2$
n = 4, dppb(Au- p tc)$_2$

n = 3, dppp(Au)$_2$(pdt)
n = 4, dppb(Au)$_2$(pdt)

Figure 2.1. Structure of phosphine gold(I) thiolate complexes studied in chapter **2.**

Ferrocenium hexafluorophosphate $[Cp_2Fe]PF_6$ was used as the oxidant in this study. Ferrocenium salts are available with a variety of counteranions including $[BF_4]^-$, $[PF_6]^-$, $[SbF_6]^-$, and $[BPh_4]^-$. The ferrocenium ion, $[Cp_2Fe]^+$, is a mild one–electron oxidant and usually is regarded as an outer – sphere reagent.' It has a broad application in stoichiometric reactions and redox catalysis. The oxidation potential of the ferrocenium

ion can be systematically altered by ring substitution providing a range of oxidants with $E^{o'}$ values varying from – 0.63 to 0.64 V (vs. Cp_2Fe). The crystalline salt of $[Cp_2Fe]PF_6$ is thermally stable and can be stored in air for several months analytically pure (C and H analysis).[5] Ferrocenium ions can be used with a wide range of polar organic solvents including CH_2Cl_2, THF, MeOH, acetone, and MeCN.[5] The solubility of the ferrocenium salt depends on the solvent and the counteranion. However the use of a solution of a ferrocenium salt is unnecessary in many cases and the solid oxidant is added directly to a solution of the substrate. Therefore the solvent choice depends on the solubility of the substrate or the stability of the product. The byproduct, ferrocene (Cp_2Fe) can be isolated by washing the product with a non-polar solvent such as hexane. However, it can be difficult to remove the excess of ferrocenium salt fiom an ionic product.[5]

Experimental Section

Reagents. Thiodiethanol, bis(diphenylphosphino)propane, bis(diphenylphosphino) butane, ferrocenium hexafluorophosphate, *p*-thiocresol, and 1,3-propanedithiol were purchased from Aldrich. Dichloromethane, chloroform and hexane were purchased from EM Sciences. Hydrogen tetrachloroaurate was purchased from Aithaca. Ethylether was purchased from VWR Scientific products. Deuterated solvents, CD_2Cl_2 and $CDCl_3$, were purchased from Cambridge Isotope. Solvents for electrochemical studies were used without further purification. Methylene chloride, HPLC grade, and the supporting electrolyte, tetra-N-butylammonium hexafluorophosphate, Bu_4NPF_6, were purchased from Aldrich.

Abbreviations. dppm = bis(diphenylphosphine)methane, dppe = bis(diphenylphosphine) ethane, dppp = bis(diphenylphosphine)propane, dppb= bis(diphenylphosphine) butane. p-tc = p-thiocresol, pdt = propane dithiolate, rev = reversible, irr = irreversible.

Instrumentation. NMR data was obtained on a Varian 300 MHz FT-NMR spectrometer (300.1MHz for ^{1}H NMR, 121.4 MHz for $^{31}P\{^{1}H\}$ NMR). All compounds were dissolved in $CDCl_3$ or CD_2Cl_2 for ***NMR*** studies. Phosphorus shifts were referenced to external concentrated phosphoric acid (85%) at 0 ppm. Elemental analysis were carried out by Desert Analytics, AZ.

Cyclic Voltammetry (CV) Experiments. CV experiments were conducted using an EG&G Princeton Applied Research 273 potentiostat/galvanostat under computer control. CV measurements were performed in methylene chloride with 0.1 M Bu_4NPF_6 as supporting electrolyte. Fresh solutions containing electrolyte (10 ml) were prepared prior to each CV experiment. Each solution was deoxygenated **by** purging with nitrogen for 2-5 minutes. Background CV's were acquired before the addition of gold complex. A three-electrode system was used, comprised of a platinum (1.6 mm diameter) working electrode, a platinum wire auxiliary electrode, and a silver/silver chloride (Ag/AgCl) reference electrode (Figure **2.2).** The working electrode was wiped prior to each experiment. The auxiliary electrode was lightly sanded before each set of experiments with fine sandpaper. Potentials are reported vs. Ag/AgCl at room temperature and are not corrected for junction potentials. Each CV experiment was repeated three times.

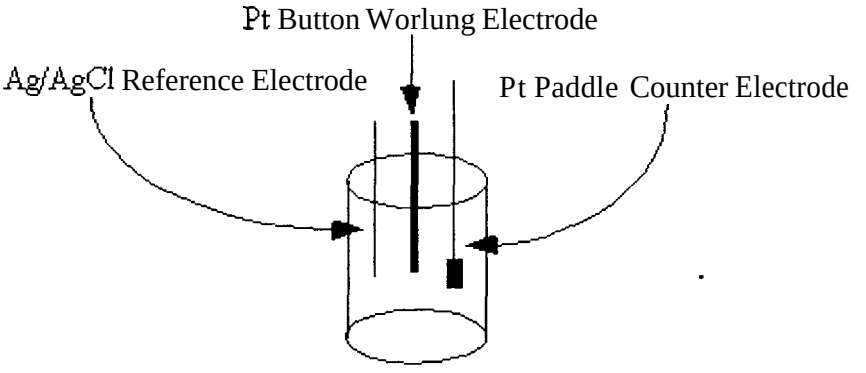


Figure 2.2. Cell for cyclic voltammetry experiments.

Preparation of dpppAu$_2$($SC_6H_4CH_3$)$_2$ and dppbAu$_2$($SC_6H_4CH_3$)$_2$.

2,2'-thiodiethanol (0.76 ml, 7.6 mmol) dissolved in 5 ml methanol was added over 10 minutes to a yellow solution of $HAuCl_4.3H_2O$ (1000 mg, 2.5 mmol) in 15 ml H_2O and 15 ml methanol. The solution was stirred in an ice bath until it became colorless. Phosphine, dppp (515 mg, 1.25 mmol) in 15 ml methanol and 15 ml $CHCl_3$ was added to the colorless solution and a white precipitate formed immediately. Methanol (40 ml) was added to complete the precipitation. The solid product, dpppAu$_2$Cl$_2$, was collected on a sintered glass frit, and washed with a total of 20 ml of methanol and air-dried.

$HSC_6H_4CH_3$ (280 mg, 2.28 mmol) was dissolved in 5 ml of ethanol and 2.28 ml 1.0M NaOH. After stirring in an ice bath for 30 min, it was slowly added to a solution of dpppAu$_2$Cl$_2$ (1.00 g, 1.14 mmol) in 250 ml CH_2Cl_2. The resulting solution was stirred for 3 hours and the volume was reduced *in vacuo*. The resulting solid was filtered and washed with ethanol (2X) and diethyl ether (2X). The product was purified by repeated

recrystallization from CH_2Cl_2/Et_2O (or CH_2Cl_2/hexanes). Total yield 88% (after recryst) **dppb$Au_2(SC_6H_4CH_3)_2$** was prepared by the same procedure. Total yield 85% (after recryst).

Oxidation of dppp$Au_2(SC_6H_4CH_3)_2$

The white solid, dppp$Au_2(SC_6H_4CH_3)_2$ (470 mg, 0.447 mmol) was dissolved in 150 ml CH_2Cl_2, and $[Cp_2Fe][PF_6]$ (148 mg, 0.447 mmol) was added as a fine blue powder. The resulting solution was stirred for 24 hours until the reaction mixture was yellow. The solvent was removed *in vacuo* and the solid residue was dissolved in 5 ml of CH_2Cl_2. 25 ml of Et_2O was added to precipitate the product. The solid was collected by filtration, and was recrystallized from CH_2Cl_2/Et_2O two times. Total yield 50 % (after recryst). The ^1H NMR ($CDCl_3$) of **[dppp$Au_2(SC_6H_4CH_3)]_2(PF_6)_2$ (1)** is shown in Figure **2.3** and the $^{31}P\{^1H\}$NMR is shown in Figure **2.4.** ^1H ***NMR*** 6 7.3-7.8 (m, 22H, $Ph_2PCH_2CH_2CH_2PPh_2$ and o-H in $SC_6H_4CH_3$), 7.06 (d, 2H, ***m-H*** in $SC_6H_4CH_3$), 3.0 (broad, 4H, $PPh_2CH_2CH_2CH_2PPh_2$) 2.35 (s, 3H, CH_3), 2.14 (broad, 2H, $PPh_2CH_2CH_2CH_2PPh_2$). $^{31}P\{^1H\}$ NMR ($CDCl_3$) 6 42.1 s, 27.7, 32.8 s, -143 (septet, PF_6). Elemental analysis calcd for **[dppp$Au_2(SC_6H_4CH_3)]_2(PF_6)_2$ (1):** C, 38.00; H, 3.10. Found: C, 37.78; H 3.08. Disulfide $(CH_3C_6H_4S)_2$ and Cp_2Fe were also found as products. These were not isolated, but were identified in the ^1H NMR of the crude reaction product, by comparison to spectra of authentic samples. $(CH_3C_6H_4S)_2$, ^1H **NMR** 2.30 (s, 6H, ***p***-CH3), 7.10 (d, 4H, *m*-H in $SC_6H_4CH_3$), 7.38 (d, 4H, o-H in $SC_6H_4CH_3$), Cp_2Fe ('HNMR 4.16, s).

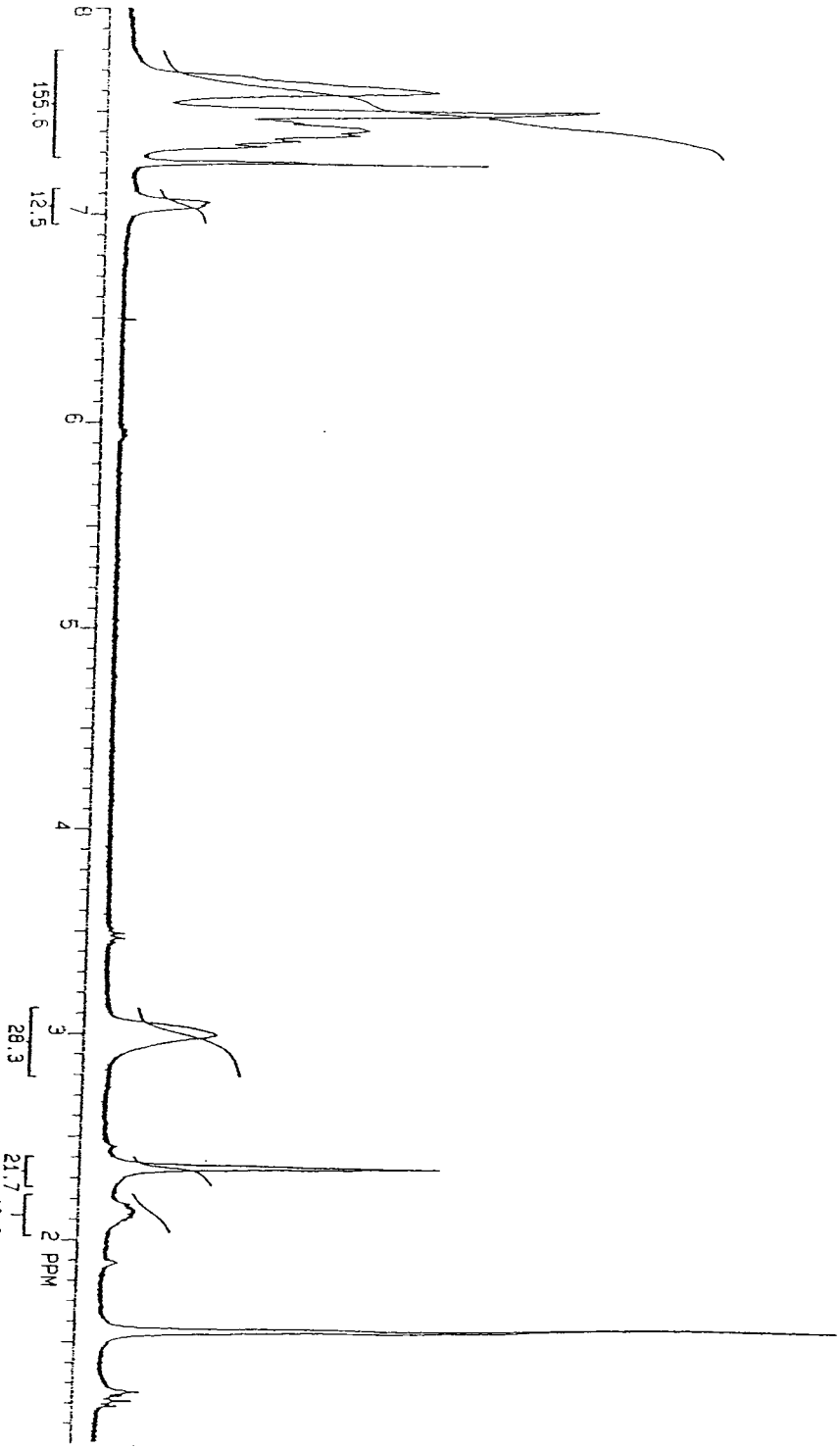


Figure 2.3. ^1H NMR spectrum of $[(dppp)_2Au_4(SC_6H_4CH_3)_2][PF_6]_2$ (1) in $CDCl_3$

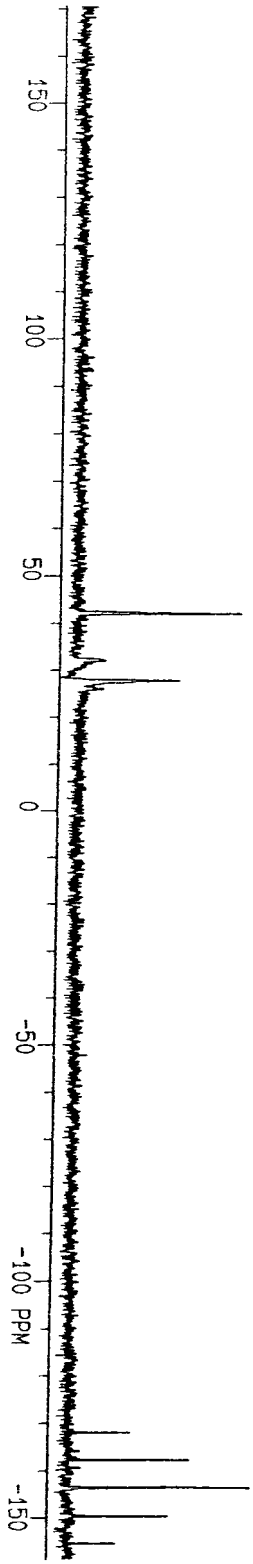


Figure 2.4. $^{31}P\{^{1}H\}$ NMR spectrum of $[(dppp)_2Au_4(SC_6H_4CH_3)_2][PF_6]_2$(1) in $CDCl_3$

The cyclic voltammogram of [dpppAu$_2$($SC_6H_4CH_3$)](PF_6) **(1)** is shown in Figure **2.5.** There is a single irreversible oxidation at approximately +1.69 V vs Ag/AgCl.

Oxidation of (dppbAu)$_2$($SC_6H_4CH_3$)$_2$ (2)

Oxidation of dppbAu$_2$($SC_6H_4CH_3$)$_2$ was carried out by the same procedure as for dpppAu$_2$($SC_6H_4CH_3$). Total yield 51 %. The 'H NMR of **[(dppbAu)$_2$($SC_6H_4CH_3$)]$_2$(PF_6)$_2$ (2)** is shown in Figure **2.6,** and the $^{31}P\{^1H\}$NMR is shown in Figure **2.7.** ^{1}H NMR ($CDCl_3$) 6 7.34-7.76 (m, 22H, $Ph_2PCH_2CH_2CH_2PPh_2$ and o-H in $SC_6H_4CH_3$), 7.05 (d, 2H, *m*-H in $SC_6H_4CH_3$), 2.67 (broad, 4H, $PPh_2CH_2CH_2CH_2CH_2PPh_2$), 2.31 (s, 3H, CH_3), 1.95 (broad, 4H, $PPh_2CH_2CH_2CH_2CH_2PPh_2$). $^{31}P\{^1H\}$ NMR 6 31.5 s, -143 (septet, PF_6). Elemental Analysis calcd for **[(dppbAu)$_2$($SC_6H_4CH_3$)]$_2$(PF_6)$_2$ (2):** C, 38.62; H, 3.24. Found: C, 38.25; H, 3.22. Disulfide $(CH_3C_6H_4S)_2$ and Cp_2Fe were also found as products.

The cyclic voltammetry of **(2)** is shown in Figure **2.8.** There is a single irreversible oxidation **at** approximately +1.6 V vs Ag/AgCl.

Preparation of [Au(dppp)(pdt)Au] and [Au(dppb)(pdt)Au].

Propane dithiol, [$HS(CH_2)_3SH$] (123.38 mg, 1.14 mmol) was dissolved in 5 ml of ethanol and 2.28 ml 1.0 M NaOH. After stirring in an ice bath for 30 min, it was slowly added to a solution of dpppAu$_2$Cl$_2$ (1.00 g, 1.14 mmol) in 250 ml CH_2Cl_2. The resulting solution was stirred for 4 hours. The volume of solution was reduced *in vacuo* and the solid product was collected by filtration and recrystallized from CH_2Cl_2/Et_2O

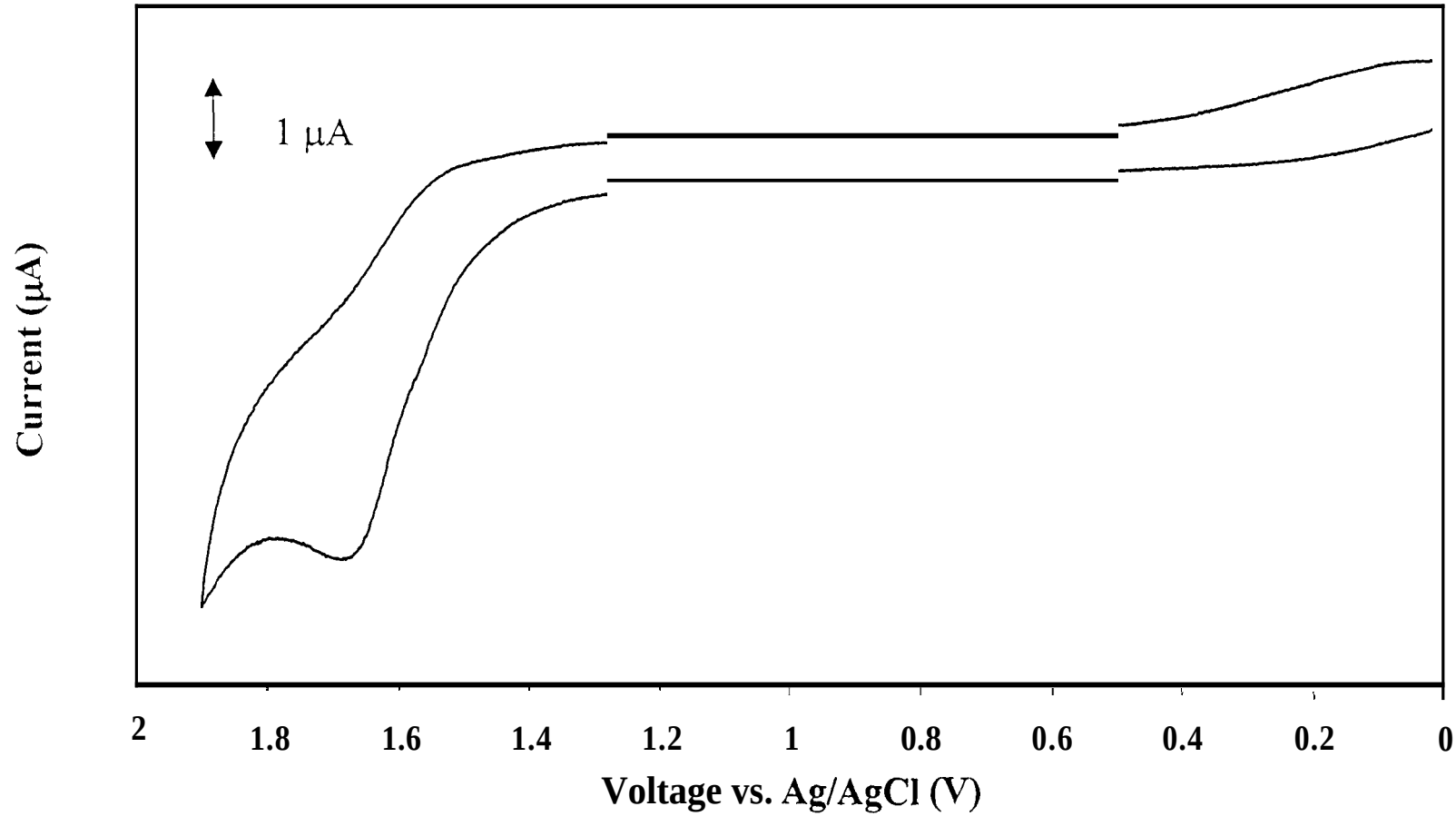


Figure 2. 5. cyclic voltammogram of 1.0 mM $[(dppp)_2Au_2(SC_6H_4CH_3)]PF_6$ in 0.1 M Bu_4NPF_6/CH_2Cl_2 at 100 mV/s.

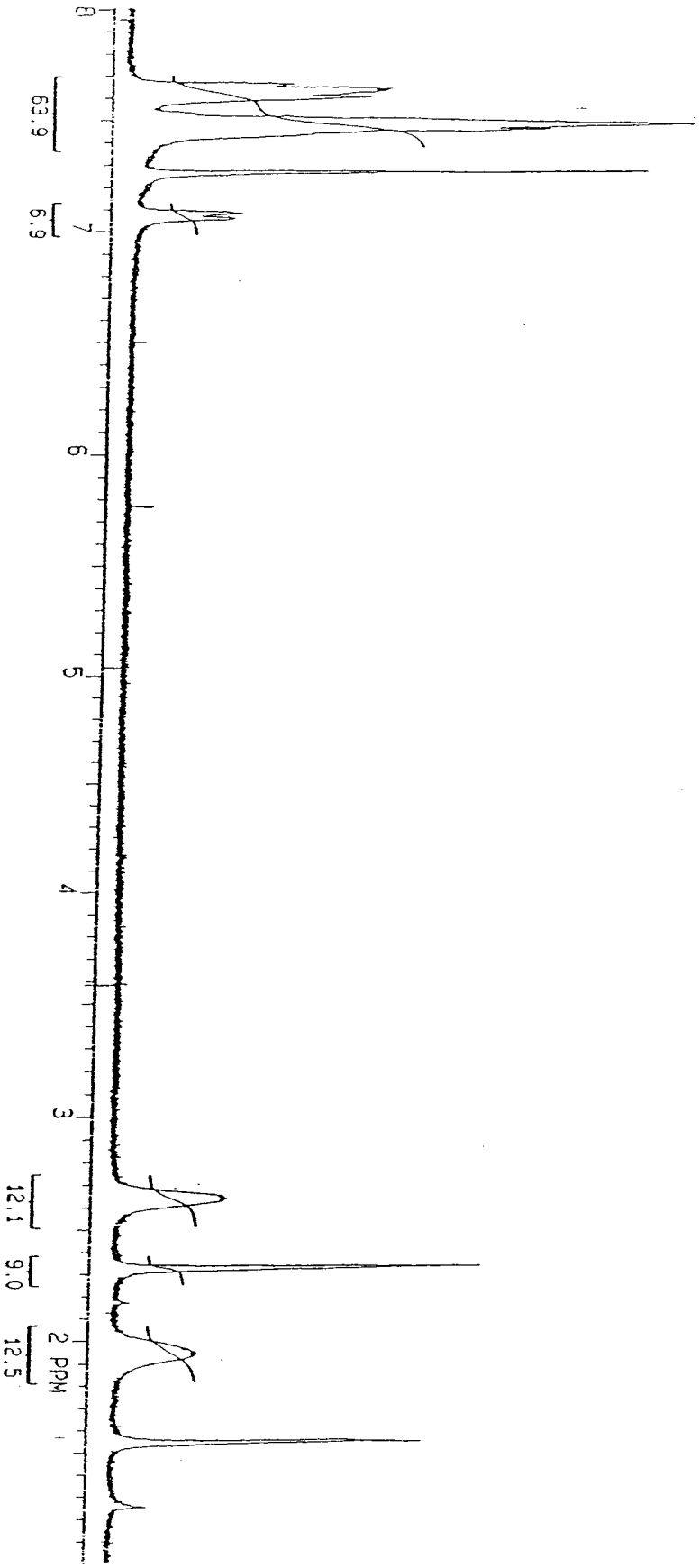


Figure 2.6. ^{1}H NMR spectrum of $[(dppb)_2Au_4(SC_6H_4CH_3)_2][PF_6]_2$ (**2**) in $CDCl_3$

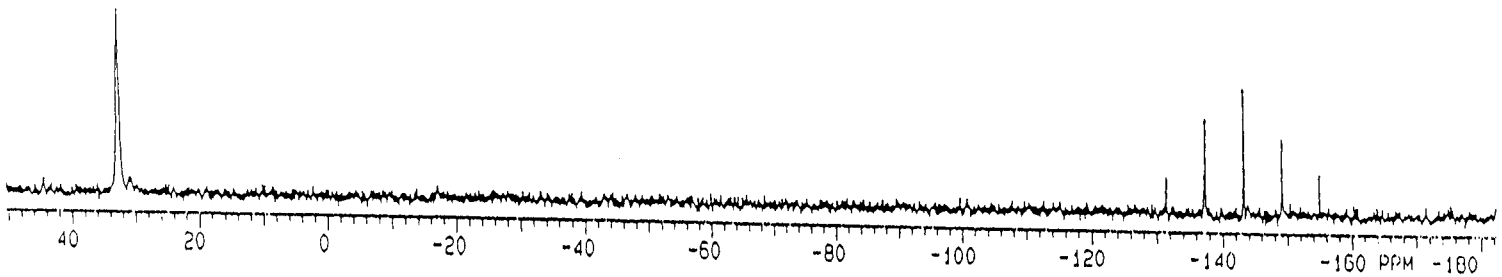


Figure 2.7. $^{31}P\{^{1}H\}$ NMR spectrum of $[(dppb)_2Au_2(SC_6H_4CH_3)_2][PF_6]_2$ (**2**) in $CDCl_3$

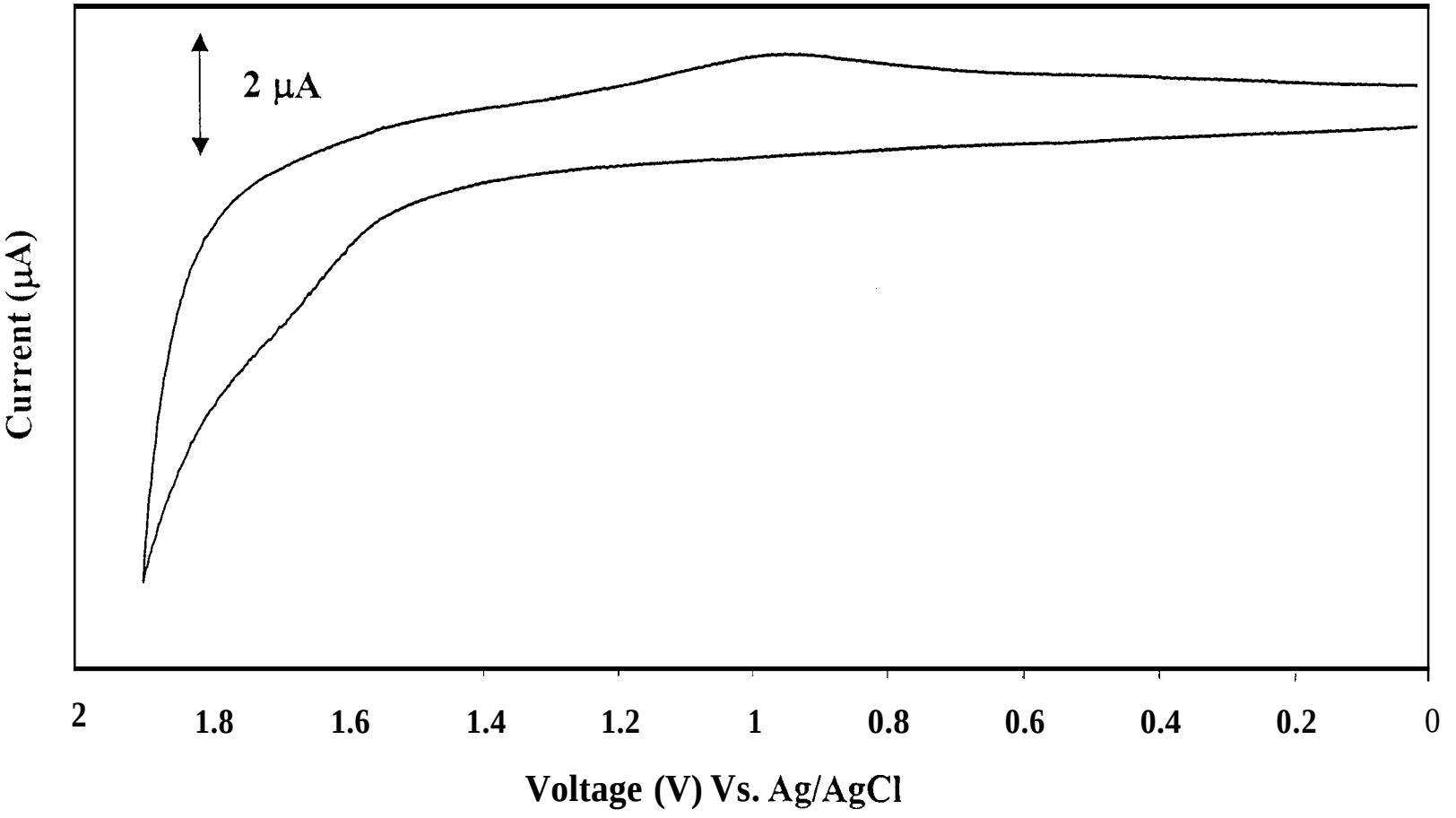


Figure 2.8. Cyclic voltammogram of 1.0 mM $[(dppb)Au_2(SC_6H_4CH_3)]PF_6$ in 0.1 M Bu_4NPF_6/CH_2Cl_2 at 100 mV/s.

two times. Total yield 45 % (after recryst). [Au(dppb)(pdt)Au] was prepared by the same procedure. Total yield 40 % (after recryst).

Oxidation of [Au(dppp)(pdt)Au].

129 mg (0.141 mmol) of [Au(dppp)(pdt)Au] was dissolved in 100 ml CH_2Cl_2 Then 46.82 mg (0.141 mmol) of $[Cp_2Fe][PF_6]$ was added as a fine powder. The resulting solution was stirred for 24 hours. The solvent was removed *in vacuo* and the solid residue was dissolved in 4 ml of CH_2Cl_2. 15 ml of Et_2O was added to precipitate the product. The solid was collected by filtration, and was recrystallized from CH_2Cl_2/Et_2O two times. Total yield 40 % (after recryst).

^{1}H NMR **of $[(dppp)_2Au_4(C_3H_6S_2)][PF_6]_2$ (3)** is shown in Figure **2.9,** and the $^{31}P\{^1H\}$NMR of **(3)** is shown in Figure **2.10.** 'H ***NMR*** ($CDCl_3$) δ 7.05-7.7 (m, 40H, 2 $Ph_2PCH_2CH_2CH_2PPh_2$), 3.48 (broad, 4H, $SCH_2CH_2CH_2S$), 2.9 (broad, 8H, 2 $Ph_2PCH_2CH_2CH_2PPh_2$), 2.3 (broad, 2H, $SCH_2CH_2CH_2S$), 1.96 (broad, 2H, $PPh_2CH_2CH_2CH_2PPh_2$). $^{31}P\{'H\}$ ***NMR*** δ 32.9 s, -143 (septet, PF_6). Elemental analysis calcd for **$[(dppp)_2Au_4(C_3H_6S_2)][PF_6]_2$ (3):** C, 33.78; H, 2.98. Found: C, 33.56; H, 2.61. Disulfide ($SCH_2CH_2CH_2S$) and Cp_2Fe were also found as products. These were not isolated, but were identified by 'H NMR of the crude reaction product. Disulfide $SCH_2CH_2CH_2S$:[4] ^{1}H NMR δ 3.1 (t, 4H, $SCH_2CH_2CH_2S$), 2.26 (q, 2H, $SCH_2CH_2CH_2S$, Cp_2Fe ('H NMR 4.2, s).

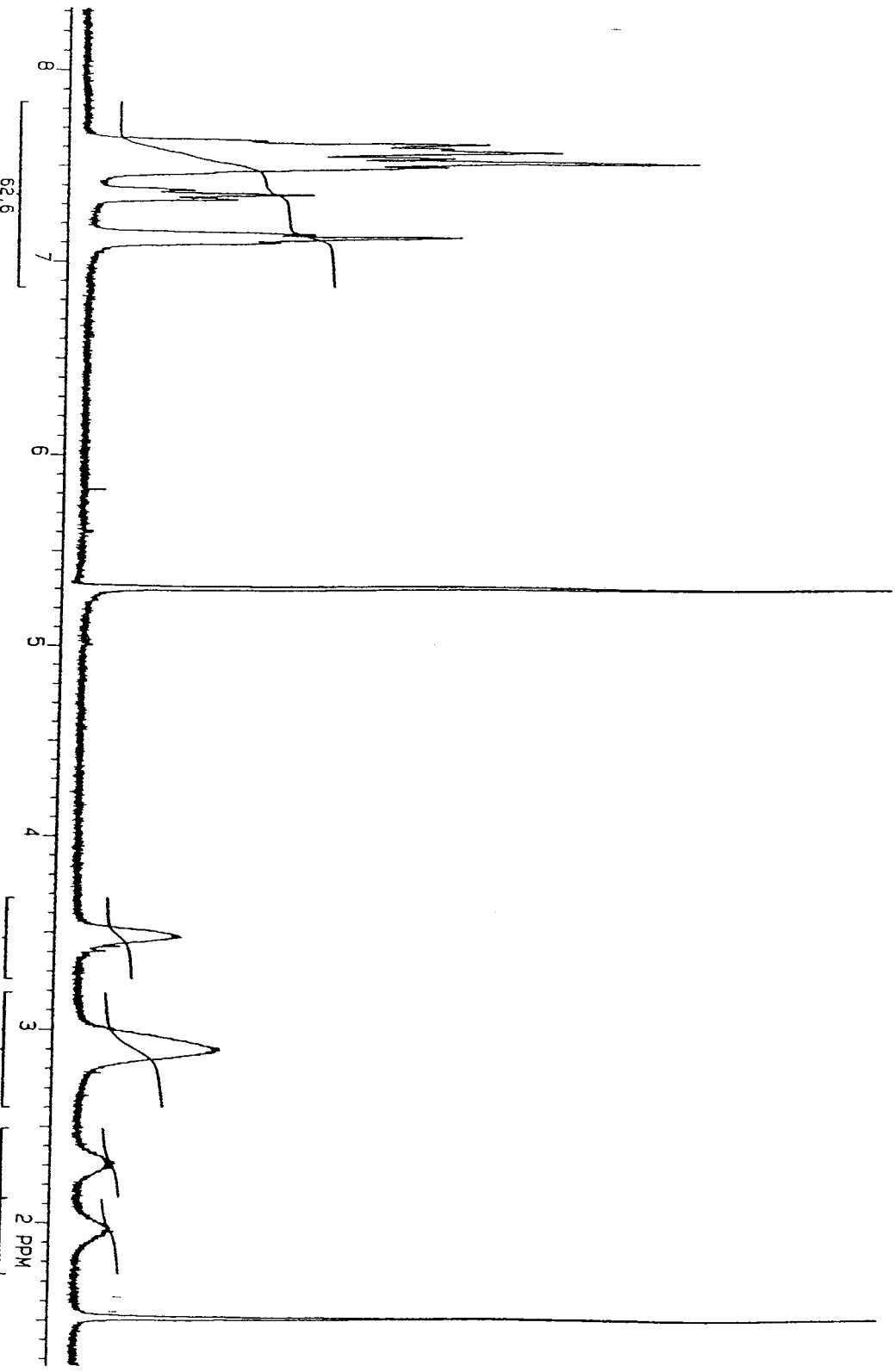


Figure 2.9. ^{1}H NMR spectrum of $[(dppp)_2Au_4(C_3H_6S_2)][PF_6]_2 \cdot H_2O$ (3) in CD_2Cl_2

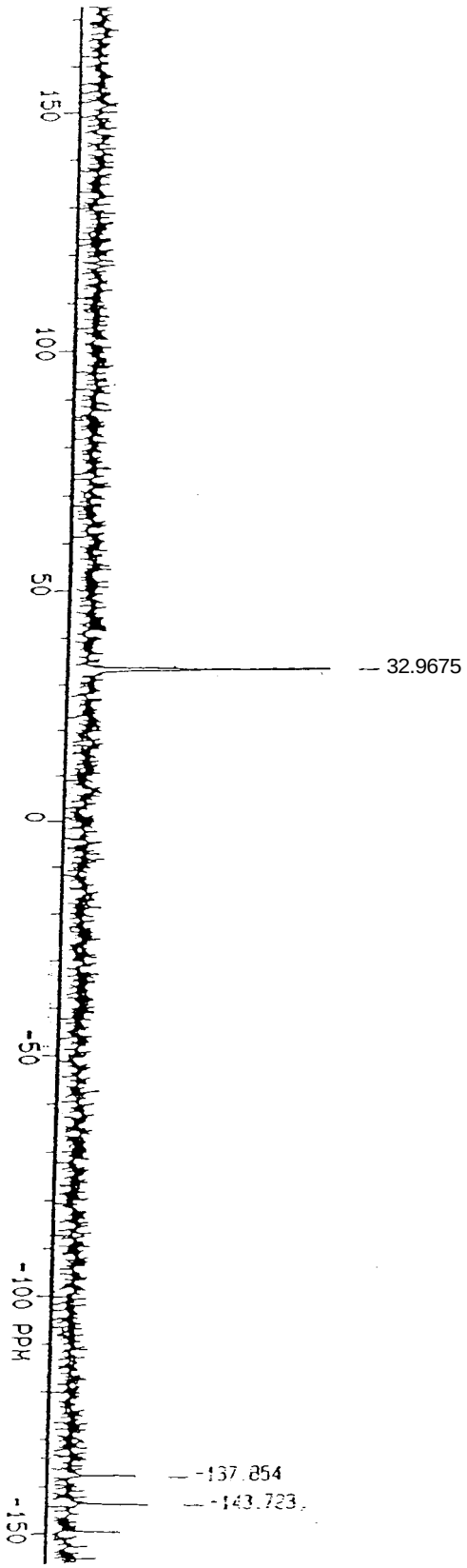


Figure 2.10. $^{31}P\{^{1}H\}$ NMR spectrum of $[(dppp)_2Au_4(C_3H_6S_2)][PF_6]_2$. (3) in CD_2Cl_2

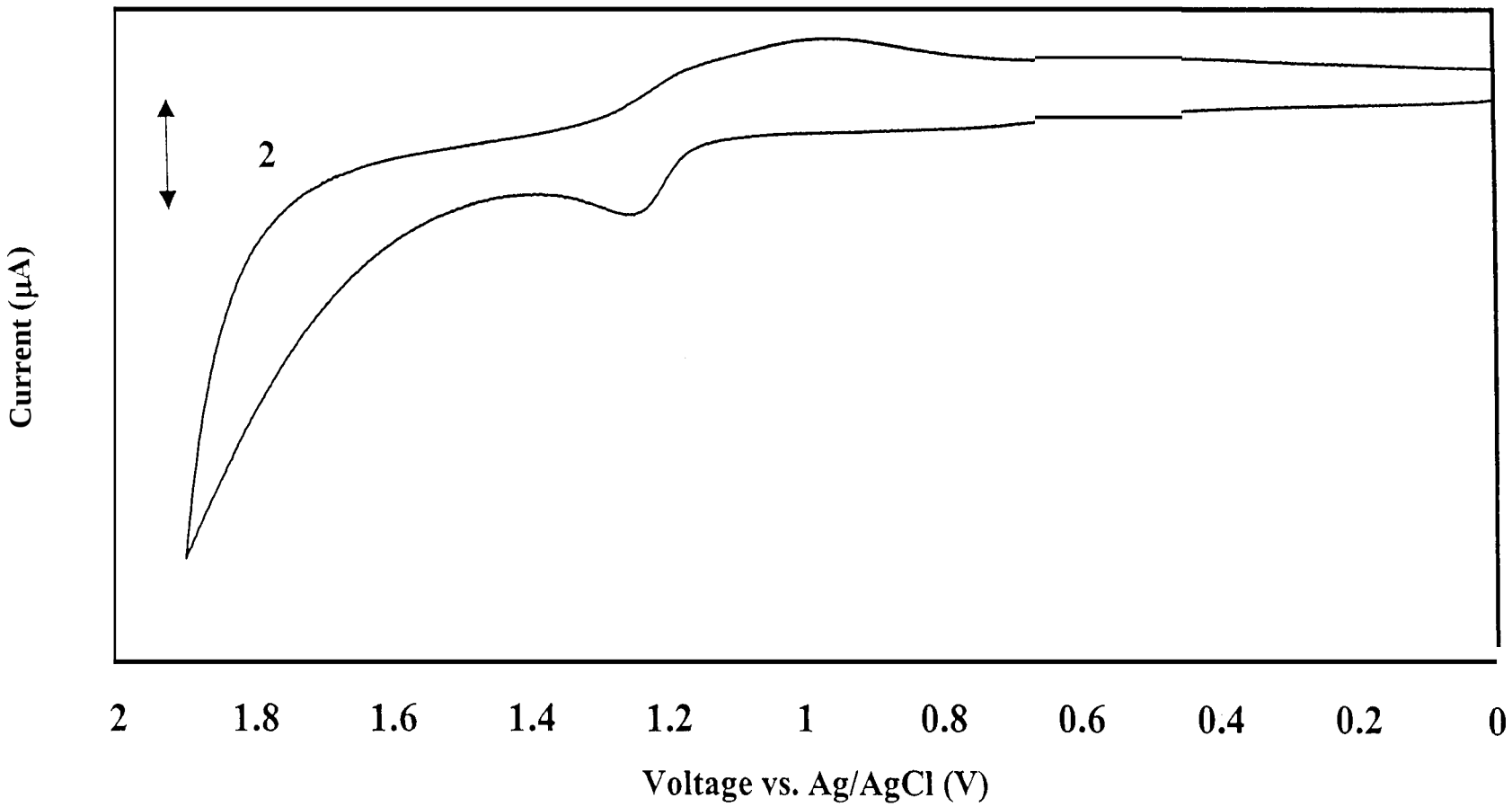


Figure 2. 11. Cyclic voltammogram of 1.0 mM $[(dppp)_2Au_4(SC_3H_6S)](PF_6)_2$ in 0.1 mM Bu_4NPF_6/CH_2Cl_2 at 100 mV/s.

The cyclic voltammetry of $[(dppp)_2Au_4(C_3H_6S_2)][PF_6]_2.H_2O$ (**3**) is shown in Figure **2.11.** There is a single irreversible oxidation at approximately +1.24 V vs Ag/AgCl.

Oxidation of [Au(dppb)(pdt)Au].

Oxidation of [Au(dppb)(pdt)Au] was carried out using the same procedure used in oxidation of [Au(dppp)(pdt)Au]. Total yield 40%. The ^1H NMR of **$[(dppb)_2Au_4(C_3H_6S_2)][PF_6]_2$ (4)** is shown in Figure **2.12,** and the $^{31}P\{^1H\}$NMR is shown in Figure **2.13.** ^1H NMR ($CDCl_3$) 6 7.3-7.8 (m, 40H, 2 $Ph_2PCH_2CH_2CH_2CH_2PPh_2$), 3.8 (broad, 4H, $SCH_2CH_2CH_2S$), 2.54 (broad, 8H, 2 $Ph_2PCH_2CH_2CH_2CH_2PPh_2$), 2.22 (broad, 2H, $SCH_2CH_2CH_2S$), 1.82 (broad, 8H, $Ph_2PCH_2CH_2CH_2CH_2PPh_2$). $^{31}P\{^1H\}$ NMR 6 30.71 s, -143.89 (septet, PF_6). Elemental analysis calcd for **$[(dppb)_2Au_4(C_3H_6S_2)][PF_6]_2$ (4):** C, 34.79; H, 3.07. Found: **C,** 34.80%; H, 2.97. Disulfide ($SCH_2CH_2CH_2S$) and Cp_2Fe were also found as products.

The cyclic voltammetry of $[(dppb)_2Au_4(C_3H_6S_2)][PF_6]_2$ **(4)** is shown in Figure **2.14.** There is a single irreversible oxidation at approximately +1.24 V vs. Ag/AgCl.

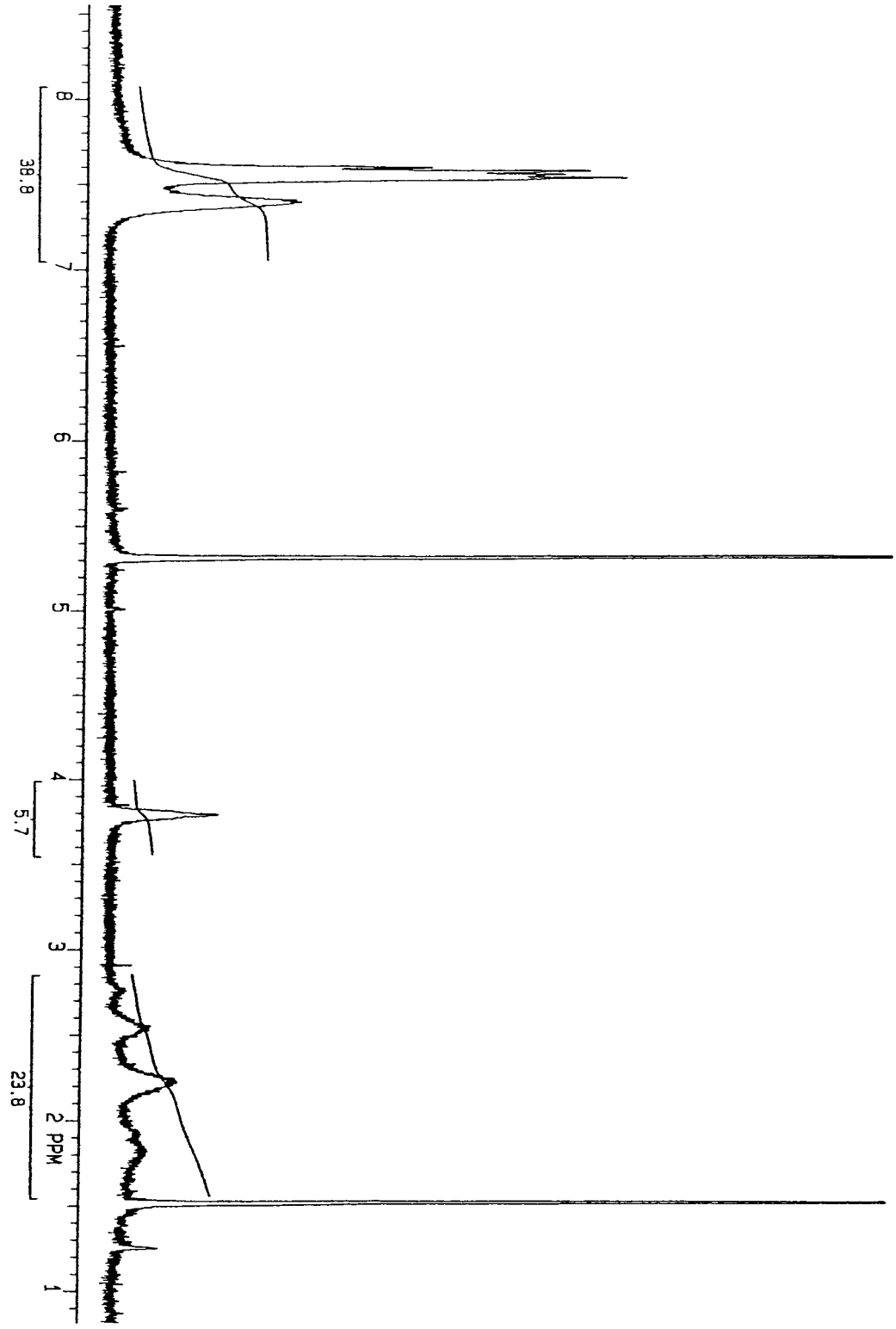


Figure 2.12. ^{1}H NMR spectrum of $[(dppb)_2Au_4(C_3H_6S_2)][PF_6]_2$ (**4**) in CD_2Cl_2

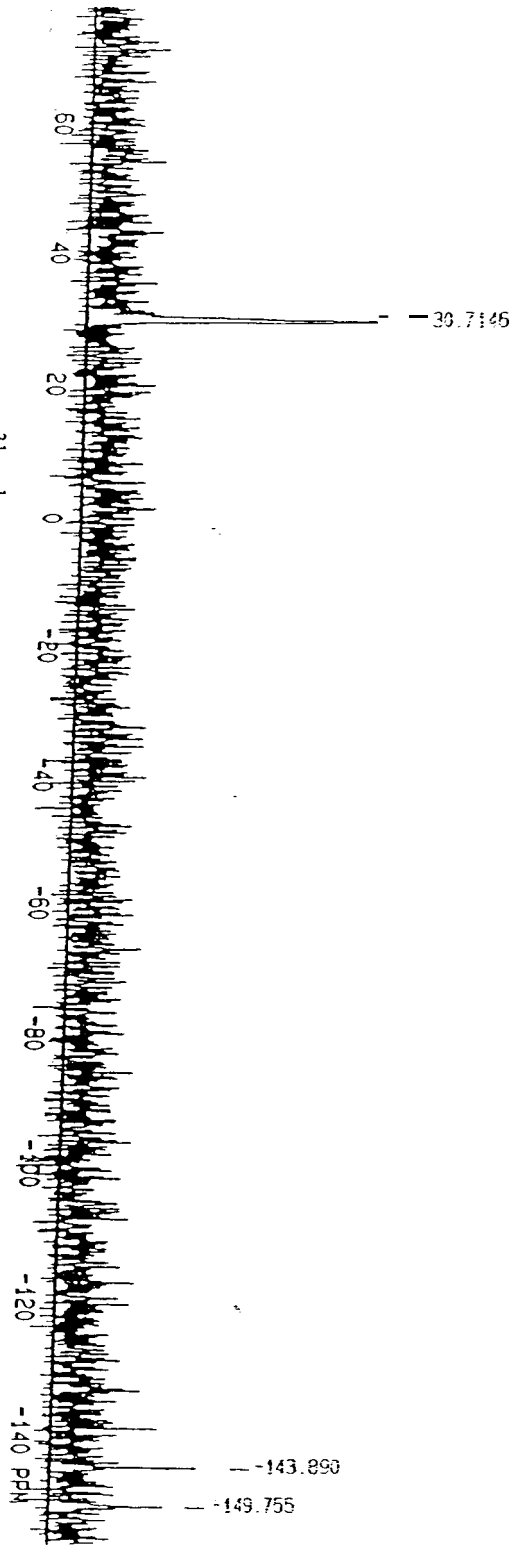


Figure 2.13. $^{31}P\{^{1}H\}$ NMR spectrum of $[(dppb)_2Au_4(C_3H_6S_2)][PF_6]_2$. (4) in CD_2Cl_2

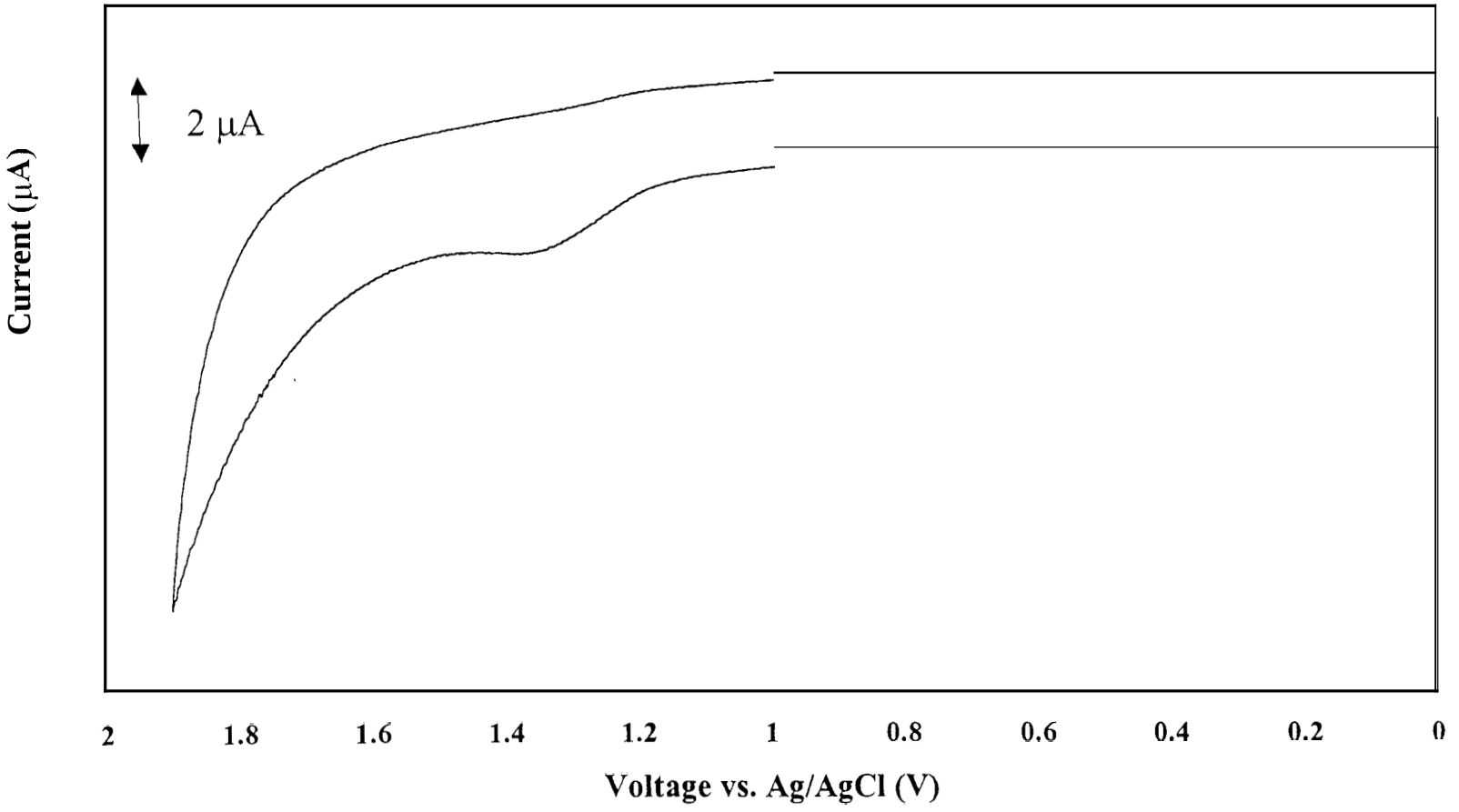


Figure 2.14. Cyclic voltammogram of 1.0 mM $[(dppb)_2Au_4(SC_3H_6S)](PF_6)_2$ in 0.1 mM Bu_4NPF_6/CH_2Cl_2 at 100 mV/s.

Results and Discussion

Chen, et al. previously reported that oxidation of $Ph_3PAuSC_6H_4CH_3$ using $[Cp_2Fe]PF_6$ as the oxidant resulted in formation of a gold(I) cluster, disulfide, and Cp_2Fe according to Equation 2.1.[2,3]

$$2Ph_3PAuSC_6H_4CH_3 + [Cp_2Fe]PF_6 \longrightarrow [(Ph_3PAu)_2(SC_6H_4CH_3)]PF_6 + 0.5\ CH_3C_6H_4SSC_6H_4CH_3 + Cp_2Fe \qquad \textbf{2.1}$$

The dinuclear gold complex subsequently dimerizes to form a tetranuclear gold(I) cluster whose structure is shown in Figure 2.15. The Au_4S_2 core adopts a chair configuration with a Au. . . Au distance of approximately **3.0** Å and a sulfur bridged, non-bonded Au. . .Au distance of **3.8** Å. Similar results from oxidation reactions of Auranofin and the PMe_3 analogue of Auranofin have been reported by another student in our group.[6]

Chen, et al. also reported the oxidation of $(dppe)Au_2(SC_6H_4CH_3)$ which proceeds in a similar fashion as the mononuclear complex to give the tetranuclear gold(I) complex shown in Figure **2.16**.[2,3]

In this chapter, the oxidation of four additional neutral gold(I) complexes is reported. There are two complexes containing *p*-thiocresolate ($SC_6H_4CH_3$), the same thiolate used in Chen's studies, and two complexes contain propane dithiolate ($SCH_2CH_2CH_2S$) (see Figure **2.1**).[2,3]

The procedure followed was similar to that reported by Chen, et al. Thus, addition of $[Cp_2Fe]PF_6$ to the dinuclear gold(I) complexes in a 1:1 molar ratio

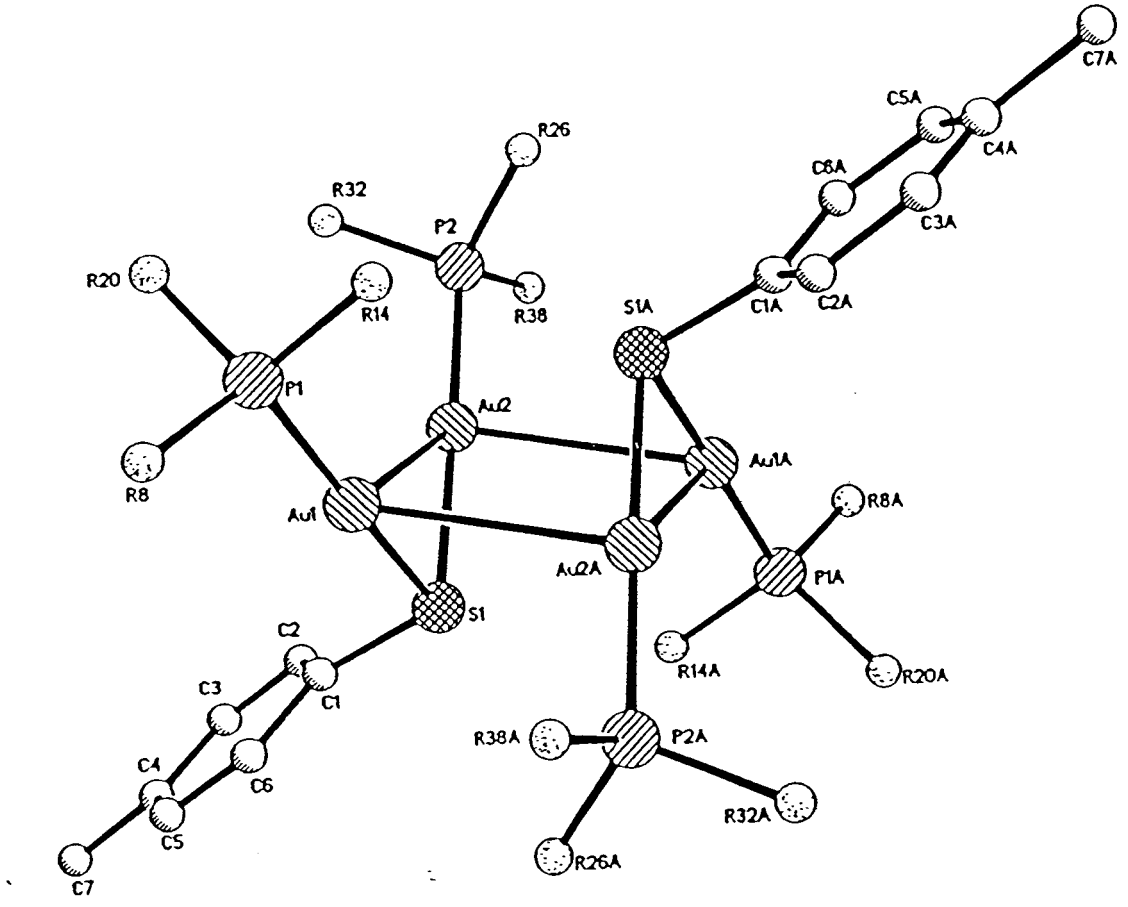


Figure 2.15. Crystal structure **of** $[(Ph_3P)_2Au_4(SC_6H_4CH_3)_2[PF_6]_2$. Phenyl rings on P and PF_6^- anions are omitted **for** clarity.[2]

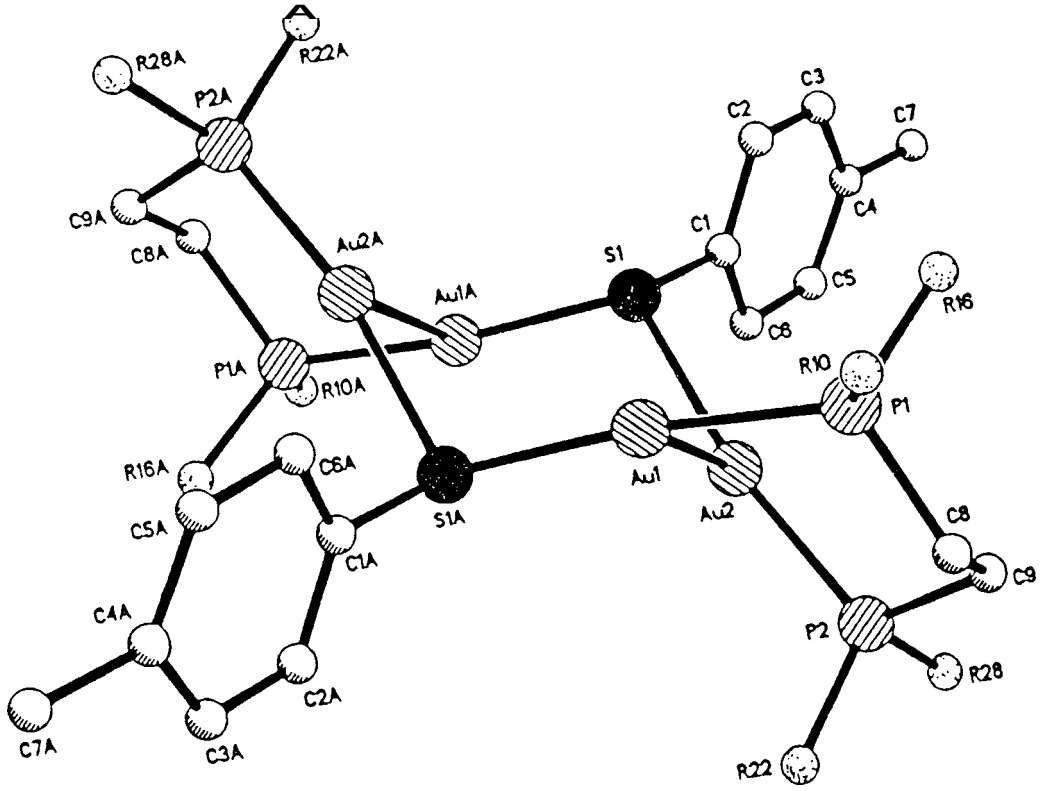


Figure 2.16. Crystal structure of $[(dppe)_2Au_4(SC_6H_4CH_3)_2[PF_6]_2$. Phenyl rings on P and PF_6^- anions are omitted for clarity.[2]

[1 $[Cp_2Fe]^+$: 2 Au(I)] resulted in the formation of gold clusters, disulfide, and ferrocene according to Equations **2.2** and **2.3.**

$$LLAu_2(SC_6H_4CH_3)_2 + [Cp_2Fe]PF_6 \longrightarrow$$

$$0.5\ [(LL)_2Au_4(SC_6H_4CH_3)_2](PF_6)_2 + 0.5\ CH_3C_6H_4SSC_6H_4CH_3 + Cp_2Fe \qquad \textbf{2.2}$$

LL = dppp,dppb

$$LLAu_2(SCH_2CH_2CH_2S) + [Cp_2Fe]PF_6 \longrightarrow$$

$$0.5\ [(LL)_2Au_4(SCH_2CH_2CH_2S)](PF_6)_2 + 0.5\ \overline{SCH_2CH_2CH_2S} + Cp_2Fe \qquad \textbf{2.3}$$

LL = dppp,dppb

The disulfides and ferrocene were identified by 'H NMR. Total yields for these products were not determined.

The clusters were isolated in 40-50% yield. This yield is based on the number of mmoles of starting gold complex and is calculated assuming that a tetranuclear dicationic cluster forms. The elemental analyesis were satisfactory for the formulas as given in Equations **2.2** and **2.3,** with the exception of $[(dppp)_2Au_4(SCH_2CH_2CH_2S)](PF_6)_2$ which requires a molecule of H_2O. Water was clearly observed in the 'H NMR spectrum (1.5 ppm) but it was difficult to quantify since there was water in the ***NMR*** solvent. Several samples of crystals have been sent to Dr. J. Krause-Bauer at the University of Cincinnati, but no structures have been solved to date.

Selected spectroscopic data for all cluster compounds prepared by our research group are summarized in Table **2.1.** The neutral gold(I) starting materials are included for comparison.

The $^{31}P\{^{1}H\}$ ***NMR*** spectra of the gold(I) clusters show a general upfield shift from the starting complexes with the exception of the $[(dppp)_2Au_4(pdt)][PF_6]_2$ clusters. For example, the peak for $Ph_3PAu(SC_6H_4CH_3)$ at 39.2 shifts to 35.2 pprn in the cluster, $[(Ph_3PAu)_2(SC_6H_4CH_3)_2][PF_6]_2$. However, [Au(dppp)(pdt)Au] showed a resonance at 28.6 ppm and the cluster complex, $[(dppp)_2Au_4(pdt)][PF_6]_2$ showed a resonance at 32.9 ppm. All clusters, with the exception of $[(dppp)_2Au_4(SC_6H_4CH_3)_2](PF_6)_2$ **(1)** (vide infra) italicize, show a sharp single peak, which indicates the equivalence **of** all phosphorous atoms.

The ^{31}P ***NMR*** shows three peaks of the isolated cluster at 42.0, 32.1, 27.7 pprn and a septet at −143 pprn assigned to the PF_6^- resonance. Oxidation reaction appears to proceed similarly to the other complexes. The elemental analysis and ^{1}H NMR are consistent with the proposed formula. The ^{31}P NMR showsa peak at 32.1 pprn might be a starting material $dpppAu_2(SC_6H_4CH_3)$ which is present in the ^{1}H ***NMR*** (a small peak at 1.9 ppm). The peak at 42.0 ppm probably indicates the formation of tetrahedral gold(I) species $Au(dppp)_2^+$.[8] The peak at 27.7 ppm in **(1)** is expected to be the assigned peak for the cluster. Trials to isolate the cluster from the tetrahedral gold(I) species by dissolving the crude in different solvents and isolating the cluster were not sucsesful also trials to do very quick ^{31}P ***NMR,*** since we were thinking that the tetrahedral is forming in the solution, did not change the outcome of the results.

Table 2.1. Spectroscopic and electrochemical data for gold(I) clusters prepared by oxidation of gold(I) thiolates by $[Cp_2Fe]PF_6$.

Compound	**^{1}H NMR δ, ppm (Selected thiolate resonance)**	**^{31}P NMR δ, ppm (Phosphine)**	**E-chem.**	**Ref.**
$Ph_3PAuSC_6H_4CH_3$	6.93 (d, 2H) 2.26 (s, 3H, CH3)	39.2	0.82 1.52	4,7
$[(Ph_3PAu)_2(SC_6H_4CH_3)_2][PF_6]_2$	7.12 (d, 2H) 2.35 (s, 3H, CH3)	35.2	1.6	2,3
$dppeAu_2(SC_6H_4CH_3)_2$	6.92 (d, 4H) 2.26 (s, 6H)	36.9	0.72 1.54	4,7
$[(dppe)_2Au_4(SC_6H_4CH_3)_2][PF_6]_2$	7.03 (d, 2H) 2.34 (s, 3H, CH_3)	33.1	1.6	2.3
$dpppAu_2(SC_6H_4CH_3)_2$	6.89 (d, 4H) 2.25 (s, 6H, CH_3)	32.0	0.77 1.54	4,7
$[(dppp)_2Au_4(SC_6H_4CH_3)_2][PF_6]_2$ (**1**)	7.06 (d, 2H) 2.35 (s, 3H, CH_3)	42.0, 32.1, 27.7	1.69	This work
$dppbAu_2(SC_6H_4CH_3)_2$	6.57 (d, 4H) 2.25 (s, 6H, CH_3)	34.9	0.83 1.59	4,7
$[(dppb)_2Au_4(SC_6H_4CH_3)_2][PF_6]_2$ (**2**)	7.05 (d, 2H) 2.31 (s, 3H, CH_3)	32.6	1.6	This work

Table 2.1 cont'd

[Au(dppp)($C_3H_6S_2$)Au]	3.45 (t, 4H) 2.05 (m,2H)	28.6	0.94 1.24	4,7
[(dppp)$_2$Au$_4$($C_3H_6S_2$)][PF_6]$_2$ (**3**)	3.48 (b, 4H) 2.3 (b, 2H)	32.96	1.24	This work
[Au(dppb)($C_3H_6S_2$)Au]	3.36 (t, 4H) 2.25 (quin, 2H	33.5	0.78 1.23	4,7
[(dppb)$_2$Au$_4$($C_3H_6S_2$)][PF_6]$_2$ (**4**)	3.8 (b, 4H) 2.22 (b, 2H)	30.7	1.24	This work

Probing the change in the environment around the thiolate ligands by using 'H NMR is an effective approach for monitoring the course of the oxidation reaction. For complexes containing the doublet assigned to the meta protons on the aromatic ring and the sharp singlet for the methyl group in *p*-tc ligand, both shift downfield from the starting gold(I) thiolates to the clusters. The doublet at 6.57 pprn and the singlet at 2.25 ppm in $dppbAu_2(SC_6H_4CH_3)_2$ were shifted to 7.8 and 2.37 ppm, respectively in the $[(dppb)_2Au_4(SC_6H_4CH_3)_2][PF_6]_2$. In the complexes with propane dithiolate ligands the triplet resonance was monitored. For example, [Au(dppb)(pdt)Au]showed a triplet at 3.36 which shifted to 3.80 ppm in $[(dppb)_2Au_4(pdt)][PF_6]_2$.

Cluster complexes containing the *p*-thiocresolate ligand show a single irreversible oxidation at - +1.6 V vs. Ag/AgCl. Compare this to neutral gold(I) thiolate complexes, in which the first oxidation occurs at –0.8 V and was assigned as oxidation of the terminal thiolate ligand. The fact that the first oxidation occurs at much more positive potentials is consistent with the increase in positive charge on the complex as well as the absence of terminal thiolate ligands in the clusters.

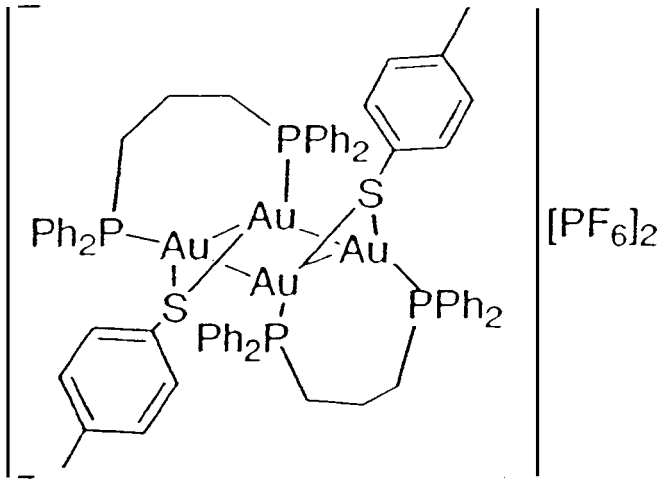
Clusters containing the propan dithiolate ligand show a single irreversible oxidation at –1.2 V vs. Ag/AgCl. The first oxidation (at –0.9 V) in the neutral, starting complexes is absent in the clusters. The fact that the first oxidation in the clusters occurs at more positive potentials is consistent with the increased positive charge and may also indicate the absence of terminal thiolate ligands.

Several attempts were made to oxidize and isolate the clusters formed from the oxidation of [Au(dppm)(pdt)Au] and [Au(dppe)(pdt)Au]. Trials to oxidize both gold(I)

thiolates using $[Cp_2Fe]PF_6$ resulted in mixed resonances in the ^1H NMR and ^{31}P NMR; although the disulfide resonances were found and the color changed from blue to yellow which suggests that the oxidation was complete. Trials to purify the clusters resulted in decomposition as evidenced by an increasing number of peaks in spectroscopic studies. Purification of the reaction products using column chromatography or recrystallization resulted in decomposition. Carrying out the oxidation in $CHCl_3$ instead of CH_2Cl_2 did not show any difference in the outcome of the reaction.

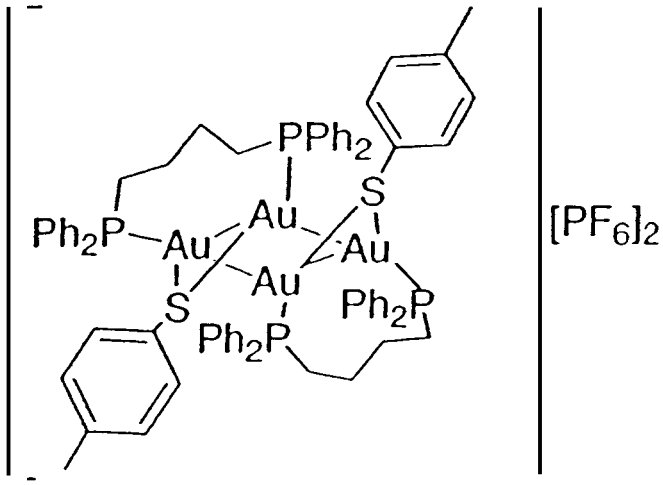
On the basis of the elemental analysis, ^1H NMR, ^{31}P NMR, and electrochemical studies, structures for the four gold cluster complexes are reported in Figures **2.17-2.20.** Each structure contains four Au(I) ions coordinated by phosphine and bridging thiolate ligands. All complexes are formulated as dications on the basis of comparison to similar structures isolated previously by Chen [2,3] and Mohamed.[6]

It will be interesting to see if X-ray structural studies confirm these proposed structures.



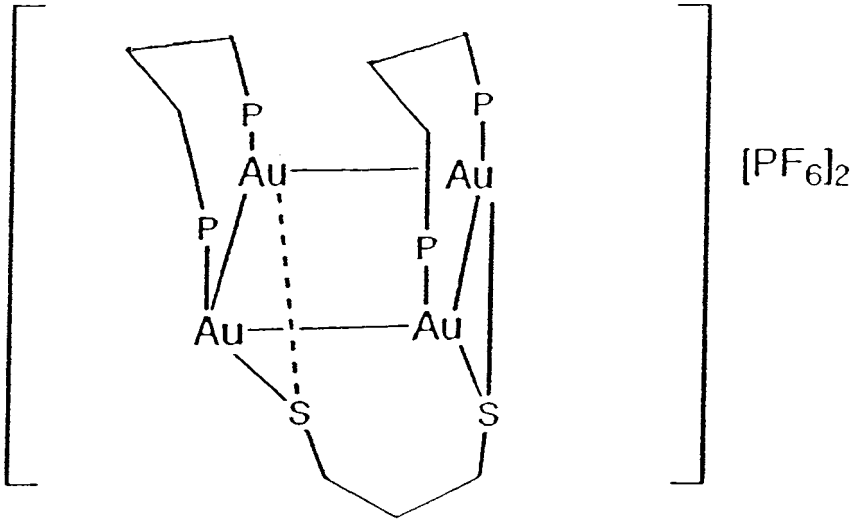
Proposed Structure

Figure 2.17. Proposed structure of $[(dppp)_2Au_4(SC_6H_4CH_3)_2][PF_6]_2$ **(1).**



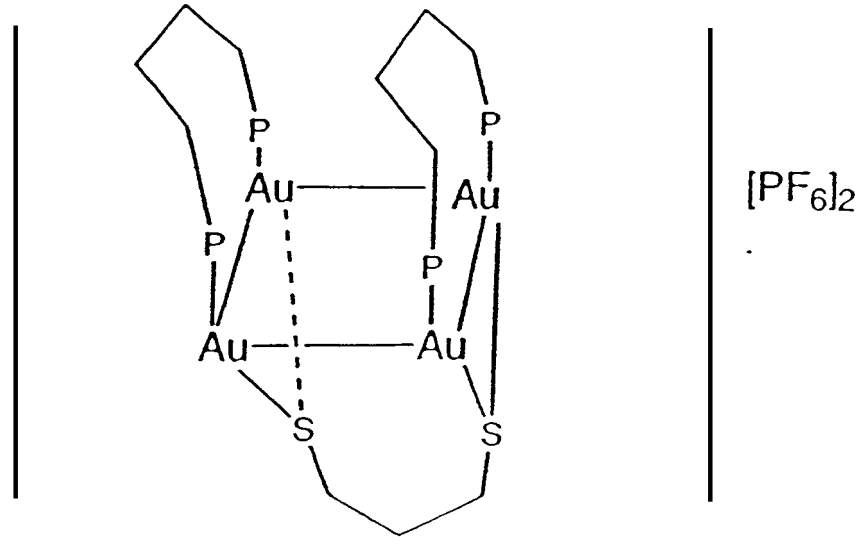
Proposed Structure

Figure 2.18. Proposed structure of $[(dppb)_2Au_4(SC_6H_4CH_3)_2][PF_6]_2$ **(2).**



Proposed Structure

Figure 2.19. Proposed structure **of** $[(dppp)_2Au_4(C_3H_6S_2)][PF_6]_2$ **(3)**



Proposed Structure

Figure 2.20. Proposed structure of $[(dppb)_2Au_4(C_3H_6S_2)][PF_6]_2$ **(4).**

References

1. Shaw, C. F., III. In *Gold: Progress in Chemistry, Biochemistry and Technology;* schmidbaur, H., Ed.; John Wiley & Sons: Chichester, **1999;** pp 250-308.

2. Chen, J.; Jiang, T.; Wei, G.; Mohamed, **A. A.;** Homrighausen, C.; Bauer, J. **A.** K.; Bruce, **A.** E.; Bruce, M. R. M. *J. Am. Chem. Soc.* **1999,121,9225-9226.**

3. Chen, J. M. Sc. thesis. University of Maine, **1999.**

4. Narayanasaswamy, R.; Young, M. **A.;** Parkhurst, E.; Ouellette, M.; Kerr, M. E.; Ho. D.; Elder, R. C.; Bruce, **A.** E.; Bruce, M. R. M. *Inorg. Chem.,* **1993,** *32,* **2506-2517.**

5. Connelly, N. G.; Geiger, W. E. *Chem. Rev.* **1996,** *96,* **877.**

6. Mohamed, **A. A.;** Bruce, **A.** E.; Bruce, M. R. M. unpublished data.

7. Jian, T.; Wei, G.; Turmel, C.; Bruce, **A.** E.; Bruce, M. R. M. *Metal-Based Drugs,* **1994,** *I,* **419-431.**

8. Mirabelli, C. K.; Hill, D. T.; Faucette, L. F.; McCabe, F. L.; Girard, G. R.; Bryan, L. B.; Sutton, B. M.; Bartus, J. O.; Crooke, **S.** T.; Johnson, R. K. *J. Med. Chem.,* **1987, 30,2181.**

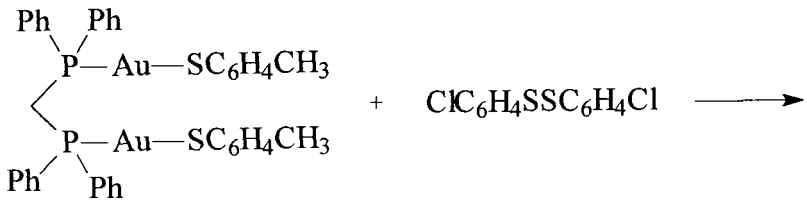
CHAPTER 3

Preliminary Kinetic Studies of the Reactions of Gold(I) Clusters with Organic Disulfides

Introduction

Studying the reaction mechanism of phosphine gold(I) thiolate complexes with disulfides has been one of our group's interests.[1,2] ^{1}H NMR experiments show that in the reaction of $dppmAu_2(SC_6H_4CH_3)_2$ (dppm = bis(diphenylphosphine)methane with $ClC_6H_4SSC_6H_4Cl$, the unsymmetrical disulfide, $ClC_6H_4SSC_6H_4CH_3$ forms first, and then the symmetrical disulfide $CH_3C_6H_4SSC_6H_4CH_3$ forms (Equations **3.1** and **3.2).**

Several other gold(I) complexes were also studied. The rate **of** reactivity of the gold thiolate complexes for this exchange reaction is: $dppmAu_2(SC_6H_4CH_3)_2$ >> $dppeAu_2(SC_6H_4CH_3)_2$ > $Ph_3PAu(SC_6H_4CH_3)$.[1] Exchange reactions of $[(Ph_3PAu)_4(SC_6H_4CH_3)_2][PF_6]_2$ with $ClC_6H_4SSC_6H_4Cl$ also showed that unsymmetrical disulfide, $ClC_6H_4SSC_6H_4CH_3$ forms first, and then the symmetrical disulfide, $CH_3C_6H_4SSC_6H_4CH_3$.[1] Preliminary kinetic studies suggested to us that complexes with Au-Au interactions, $dppmAu_2(SC_6H_4CH_3)_2$ and $[(Ph_3PAu)_4(SC_6H_4CH_3)_2][PF_6]_2$, react faster than complexes without Au-Au interactions, $Ph_3PAu(SC_6H_4CH_3)$ and $dppeAu_2(SC_6H_4CH_3)_2$.[3,4]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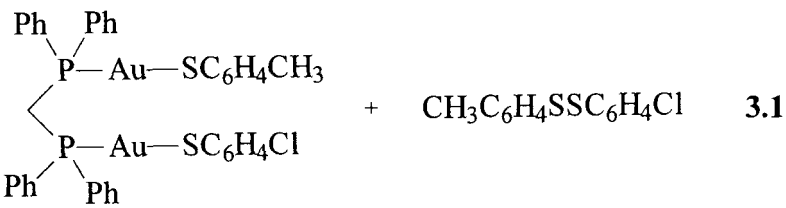
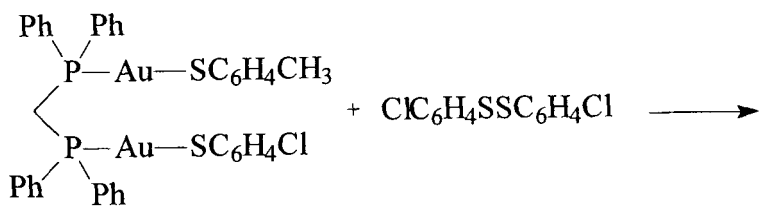
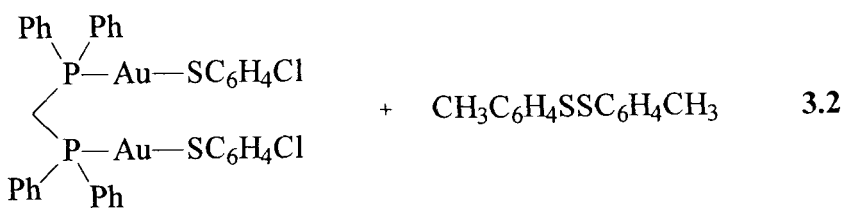
P—Au—SC6H4CH3
Ph Ph
+ ClC6H4SSC6H4Cl


Ph Ph
P—Au—SC6H4CH3
P—Au—SC6H4Cl
Ph Ph
+ CH3C6H4SSC6H4Cl

3.1


Ph Ph
P—Au—SC6H4CH3
P—Au—SC6H4Cl
Ph Ph
+ ClC6H4SSC6H4Cl


Ph Ph
P—Au—SC6H4Cl
P—Au—SC6H4Cl
Ph Ph
+ CH3C6H4SSC6H4CH3

3.2

The thiolate bridged gold cluster complexes discussed in chapter **2** have several Au-Au interactions. We were interested to test our hypothesis concerning a correlation between Au-Au bonds and the rate of reaction with disulfide. The first part of this chapter describes studies to determine the rate law of the reaction of $[(Ph_3PAu)_4(SC_6H_4CH_3)_2][PF_6]_2$ with $ClC_6H_4SSC_6H_4Cl$. This cluster complex was chosen for kinetic studies because it was well characterized[5] and it was known to react with $ClC_6H_4SSC_6H_4Cl$.[3] Kinetic data was obtained by monitoring the reaction by ^1H NMR. The change in concentrations of starting cluster or unsymmetrical disulfide were measured by the integration of the area under the methyl peaks.

The second part of this chapter describes studies to compare the rates of reaction of several cluster complexes, the neutral dinuclear complexes, $LLAu_2(SC_6H_4CH_3)$(LL = dppm, dppe) and the neutral mononuclear complex, $Ph_3PAu(SC_6H_4CH_3)$.

Experimental

Reagents. Thiodiethanol, triphenylphosphine, bis(diphenylphosphine)methane, bis(di phenylphosphine)ethane, bis(diphenylphosphine)propane, bis(diphenylphosphine)butane, $[Cp_2Fe]PF_6$, *p*-thiocresol ($HSC_6H_4CH_3$, *p*-tc), 1,3-propanedithiol ($HS(CH_2)_3SH$), dioxane ($C_4H_8O_2$), and *p*-chlorothiophenol were purchased from Adrich. Dichloromethane, chloroform, and hexane were purchased from EM Sciences. Hydrogen tetrachloroaurate was purchased from Aithaca. Ethylether, VWR micropipettes and VWR microsyringes, were purchased from VWR Scientific products. Deuterated solvents, CD_2Cl_2 and $CDCl_3$, were purchased from Cambridge Isotope. Solvents were used without further purification.

Instrumentation. NMR data was obtained on a Varian 300 MHz FT-NMR spectrometer (300.1MHz for ^1H NMR). All compounds were dissolved in CD_2Cl_2 for NMR studies.

Synthesis. $[dppmAu_2(SC_6H_4CH_3)_2]$, $[dppeAu_2(SC_6H_4CH_3)_2]$, $Ph_3PAu(SC_6H_4CH_3)$ and $[(Ph_3PAu)_4(SC_6H_4CH_3)_2][PF_6]_2$ were prepared according to previously published procedures, which is similar to the synthesis described in chapter 2.[3,6] The gold cluster $[(dppb)_2Au_4(SC_6H_4CH_3)_2][PF_6]_2$ was synthesized using the procedure described in Chapter **2.**

Disulfide Exchange Reactions. The cluster, $[(Ph_3PAu)_4(SC_6H_4CH_3)_2][PF_6]_2$ was chosen for the kinetic study. To determine the order of reaction in cluster concentration, a high concentration (40 mM) of $ClC_6H_4SSC_6H_4Cl$ was used (pseudo-first order conditions). To determine the order of reaction in disulfide, the disulfide concentration was varied from 5 mM to 20 mM while the concentration of cluster was held constant at *3* mM. Pseudo-first order conditions (i.e. a high concentration of cluster relative to disulfide) were not feasible because the CH3 peak from the cluster was so large, that as the unsymmetrical disulfide, $CH_3C_6H_4SSC_6H_4Cl$, formed, it's CH_3 peak appeared only as a small shoulder upfield of the cluster CH_3 peak. Thus it was not possible to measure separate integrals for the two CH3 peaks. In addition, if the cluster concentration was held at 3 mM and the disulfide concentration was a factor of 10 or greater (i.e. pseudo-first order in cluster) then the reaction was very slow.

The ^1H ***NMR*** was used to follow the reaction for the first *3* hours for cluster complexes and 7 hours for the neutral complexes. Dioxane $(C_4H_8O_2)$ was used initially as a standard. Control experiments demonstrated that dioxane does not react with cluster or

disulfide. However, it turned out that dioxane was not useful as a standard and it was not used in later kinetic experiments. Micropipettes and microsyringes were used to measure the volumes.

(a) Determination of the order of reaction in $[(Ph_3PAu)_4(SC_6H_4CH_3)_2][PF_6]_2$

For determination of the order of reaction in cluster concentration six different concentrations of $[(Ph_3PAu)_4(SC_6H_4CH_3)_2][PF_6]_2$ were reacted with 40 mM of bis(*p*-clorophenyl)disulfide ($ClC_6H_4SSC_6H_4Cl$) in six different ^1H NMR runs. Table **3.1** shows the different concentration combinations for each run.

General Procedures. 1. Preparation of a stock solution of **3.88** mM $[(Ph_3PAu)_4(SC_6H_4CH_3)_2][PF_6]_2$: 18.4 mg of the cluster was dissolved in a few drops of CD_2Cl_2 (enough to dissolve the solid) in small beaker then the solution was transferred to a 2.00 ml volumetric flask and the beaker was rinsed 2 to 3 times with small amounts of CD_2Cl_2 . The rinsing solution was also transferred to the same volumetric flask, then the flask was filled to the mark with CD_2Cl_2.

2. Preparation of a stock solution of 117 mM dioxane ($C_4H_8O_2$): 20 μL of dioxane was transferred to a 2.00 ml volumetric flask, then the flask was filled to the mark with CD_2Cl_2.
3. Preparation of a stock solution of 400 mM bis(*p*-clorophenyl)disulfide ($ClC_6H_4SSC_6H_4Cl$): 0.23 mg of the disulfide was dissolved in few drops of CD_2Cl_2 (enough to dissolve the solid) in a small beaker, then the solution was transferred to a 2.00 ml volumetric flask and the beaker was rinsed 2 to 3 times with small amounts

of CD_2Cl_2 . The rinsing solution was also transferred to the same volumetric flask, then the flask was filled to the mark with CD_2Cl_2.

Table **3.1.** The Experimental matrix for 6 experiments varying the concentration of $[(Ph_3PAu)_4(SC_6H_4CH_3)_2][PF_6]_2$ under pseudo first order conditions.

Experiment (initial cluster concentration)	**Volume of cluster stock solution (3.88mM)**	**Volume of dioxane stock solution (117mM)**	**Volume of disulfide stock solution (400 mM)[a]**	**Volume of CD_2Cl_2 added to make 1000 μL final volume**
Run **A** (0.35 mM cluster)	90 μL	10 μL	100 μL	800 μL
Run **B** (0.66 mM cluster)	170 μL	10 μL	100 μL	720 μL
Run **C** (1.01 mM cluster)	260 μL	10 μL	100 μL	630 μL
Run **D** (1.51 mM cluster)	390 μL	10 μL	100 μL	500 μL
Run **E** (2.02 mM cluster)	520 μL	10 μL	**100** μL	370 μL
Run **F** (3.33 mM cluster)	**860** μL	10 μL	100 μL	30 μL

Run A

90 μL from the cluster stock solution (3.88 mM) was transferred by using a micropipette to a small vial. Then 10 μL from the dioxane stock solution (117 mM) was added, followed by 800 μL of CD_2Cl_2. To this solution was added 100 μL from the disulfide stock solution (400 mM) and the time of mixing was recorded. An aliquot was

transferred to NMR tube by using a disposable glass pipette, to give a height of 5 cm in the tube. The initial concentrations of cluster, disulfide and dioxane were 0.35 mM, 40 mM, and 1.17 mM, respectively. ^{1}H NMR spectra (32 transients each) were collected over a time period of 3 hours. The NMR tube was stored at room temperature, but the temperature was not precisely controlled.

Runs **B-F** were carried out according to the data shown in Table **3.1.** Each run was duplicated, for a total of 12 experiments.

(b) Determination of the order of reaction in $ClC_6H_4SSC_6H_4Cl$ concentration

For determination of the order of reaction in disulfide concentration, three different concentrations of $ClC_6H_4SSC_6H_4Cl$ were reacted with 3.00 mM of $[(Ph_3PAu)_4(SC_6H_4CH_3)_2][PF_6]_2$ in three different 'H NMR runs **(GI).** Table **3.2** shows the different concentration combinations for each run.

1. Preparation of a stock solution of 50 mM $ClC_6H_4SSC_6H_4Cl$: 0.02 g of the disulfide was dissolved in a few drops of CD_2Cl_2 (enough to dissolve the solid) in a small beaker then the solution was transferred to a 2.00 ml volumetric flask and the beaker was rinsed 2 to 3 times with small amounts of CD_2Cl_2 . The rinsing solution was also transferred to the same volumetric flask, then the flask was filled to the mark with CD_2Cl_2.
2. Preparation of a stock solution of 5.00mM $[(Ph_3PAu)_4(SC_6H_4CH_3)_2][PF_6]_2$: 0.02 g of the cluster was dissolved in a few drops of CD_2Cl_2 (enough to dissolve the solid) in small beaker then the solution was transferred to a 2.00 ml volumetric flask and the beaker was rinsed 2 to 3 times with small amounts of CD_2Cl_2 . The rinsing solution

was also transferred to the same volumetric flask, then the flask was filled to the mark with CD_2Cl_2.

Run G

600 μL from the cluster stock solution (5.00 mM) was transferred by using a micropipette to a small vial, followed by 300 μL of CD_2Cl_2. To this solution was added 100 μL from the disulfide stock solution (50.0 mM) and the time of mixing was recorded. An aliquot was transferred to an NMR tube by using a disposable glass pipette, to give a height of 5 cm in the tube. The initial concentrations of cluster and disulfide were 3.00 mM and 5.00 mM, respectively. ^1H NMR spectra (32 transients each) were collected over a time period of **3** hours. The NMR tube was stored at room temperature, but the temperature was not precisely controlled. Runs **H** and **I** were carried out according to the data shown in Table **3.2.**

Table 3.2. The experimental matrix for runs **G, H** and **I.**

Experiment (initial disulfide concentration)	**Volume of disulfide stock solution (50.0 mM)**	**Volume of cluster stock solution(5.00 mM)[a]**	**Volume of CD_2Cl_2 added to make 1000 μL final volume**
Run **G** (5.00 mM disulfide)	100 μL	600 μL	300 μL
Run **H** (10.0 mM disulfide)	200 μL	600 μL	200 μL
Run **I** (20.0 mM disulfide)	400 μL	600 μL	000 μL

a. The initial concentration of cluster for each experiment is 3.00 mM.

(c) Comparison studies of mononuclear and dinuclear gold(I) complexes to $[(Ph_3PAu)_4(SC_6H_4CH_3)_2][PF_6]_2$

Mononuclear $Ph_3PAu(SC_6H_4CH_3)$ 3.20 mM (run **J**), dinuclear $[dppmAu_2(SC_6H_4CH_3)_2]$ 3.20 mM (run **K**), and $[dppeAu_2(SC_6H_4CH_3)_2]$ 3.20 mM (run **L**) gold(I) complexes were reacted with 40 mM of bis(*p*-clorophenyl)disulfide, $ClC_6H_4SSC_6H_4Cl$ for a Comparison Studies to Gold Cluster $[(Ph_3PAu)_4(SC_6H_4CH_3)_2][PF_6]_2$. Runs **J, K** and **L** were mixed as described previously in run ***G***. Table **3.3** shows the different concentration combinations of mononuclear, dinuclear Gold(I) complexes, and disulfide.

Table 3.3. Experimental matrix for runs **J, K** and **L** .

Experiment(initial gold(I) complexes concentration)	**Volume of gold(I) complexes stock solution (3.20 mM)**	**Volume of disulfide stock solution(400 mM)[a]**	**Volume of CD_2Cl_2 added to make 1000 µL final volume**
Run **J** ($Ph_3PAu(SC_6H_4CH_3$ 3.20 mM)	800 µL	100 µL	100 µL
Run **K** [$dppmAu_2(SC_6H_4CH_3$) 3.20 mM	800 µL	100 µL	100 µL
Run **L** [$dppeAu_2(SC_6H_4CH_3)$ 3.20 mM	800 µL	100 µL	100 µL

a. The initial concentration of disulfide for each experiment is 40.0 mM.

(d) Comparison studies of gold cluster $[(dppb)_2Au_4(SC_6H_4CH_3)_2][PF_6]_2$ to $[(Ph_3PAu)_4(SC_6H_4CH_3)_2][PF_6]_2$

Three different concentration [1.16 mM (run **M**), 2.33 mM (run **N**), and 3.10 mM (run **O**) of gold cluster $[(dppb)_2Au_4(SC_6H_4CH_3)_2][PF_6]_2$ were chosen to react with 40 mM of bis(*p*-clorophenyl)disulfide, $(ClC_6H_4SSC_6H_4Cl)$ for a comparison studies to gold Cluster $[(Ph_3PAu)_4(SC_6H_4CH_3)_2][PF_6]_2$. Run **M, N** and **O** were mixed as described previously in run **G.** Table **3.4** shows the different concentration combinations of gold cluster $[(dppb)_2Au_4(SC_6H_4CH_3)_2][PF_6]_2$ and disulfide.

Table 3.4. Experimental matrix for runs **M, N** and **O.**

Experiment(initial cluster concentration)	**Volume of cluster stock solution (3.88 mM)**	**Volume of disulfide stock solution(400 mM)[a]**	**Volume of CD_2Cl_2 added to make 1000 μL final volume**
Run **M** (1.16 mM)	300 μL	100 μL	600 μL
Run **N** (2.33 mM)	600 μL	100 μL	300 μL
Run **O** (3.10 mM)	800 μL	100 μL	100 μL

a. The initial concentration of disulfide for each experiment is 40.0 mM

Results and Discussion

Determining the order of reaction in $[(Ph_3PAu)_4(SC_6H_4CH_3)_2][PF_6]_2$

To determine the order of reaction in cluster complex, experiments were conducted under pseudo first order conditions. Thus the initial cluster concentration varied from 0.35-3.33 mM (Runs A-F) while the initial disulfide concentration was held constant at 40.0 mM. Six different concentrations of cluster were used and each run was duplicated for a total of 12 experiments. Figure **3.1** shows the ^1H NMR of $[(Ph_3PAu)_4(SC_6H_4CH_3)_2][PF_6]_2$. The ^1H NMR spectrum of the disulfide exchange reaction mixture of $[(Ph_3PAu)_4(SC_6H_4CH_3)_2][PF_6]_2$ (1.94 mM) with 40.0 mM of disulfide after 1 hour is shown in Figure **3.2.** During the reaction the methyl group signal of the gold cluster at 2.35 ppm decreases, while the methyl group signal of the disulfide at 2.31 ppm increases (Equation **3.3**).

$$[(Ph_3PAu)_4(SC_6H_4CH_3)_2](PF_6)_2 + ClC_6H_4SSC_6H_4Cl \longrightarrow$$
$$[(Ph_3PAu)_4(SC_6H_4CH_3)(SC_6H_4Cl)](PF_6)_2 + ClC_6H_4SSC_6H_4CH_3 \qquad \textbf{3.3}$$

For experiments A-F, in which the cluster concentration varied and the disulfide concentration was constant, an increase in cluster concentration lead to a proportional increase in rate. This is consistent with a reaction that is first order in cluster concentration.

The plots of ln[cluster] (M) versus time (s) (Figures **3.3-3.14)** show a linear relationship, which is consistent with first order in cluster concentration. Plots testing for

other orders did not show a good fit. The trend lines shown on each plot are calculated by Excel. Since the slopes of the trend line contain only one significant figure, another function was used to calculate slopes from the data. The average of 12 experiments is shown on Table **3.5.** The rate constant was then calculated by dividing the slope by 40.0 mM according to Equation **3.4**

$$k_{obs} = \mathbf{k}\,[ClC_6H_4SSC_6H_4Cl] \qquad \mathbf{3.4}$$

The average rate constant calculated from Equation **3.3** is **6.8** $\pm$ 1.0 x 10^{-3} M^{-1} S^{-1}.

Determining the order of reaction in disulfide

Ideally, these experiments should also have been conducted under pseudo first order conditions. However we encountered two problems with this approach as explained in the experimental section of this chapter. Thus for this set of experiments the disulfide concentration varied from 5-20 mM while the cluster concentration was held constant at **3.0** mM. Three different disulfide concentrations were used (runs G-I) and each run was done once.

For experiments **G-I,** in which the disulfide concentration varied and the cluster concentration was constant, an increase in disulfide concentration lead to a proportional increase in rate. This is consistent with a reaction that is first order in disulfide concentration. Figures **3.15-3.17** show plots **of** ln[disulfide] (M) versus time (s). The figures show a linear relationship, which is consistent with first order in disulfide concentration.

Figure 3.1. ^{1}H NMR of $[(Ph_3PAu)_4(SC_6H_4CH_3)_2][PF_6]_2$ in $CDCl_3$.

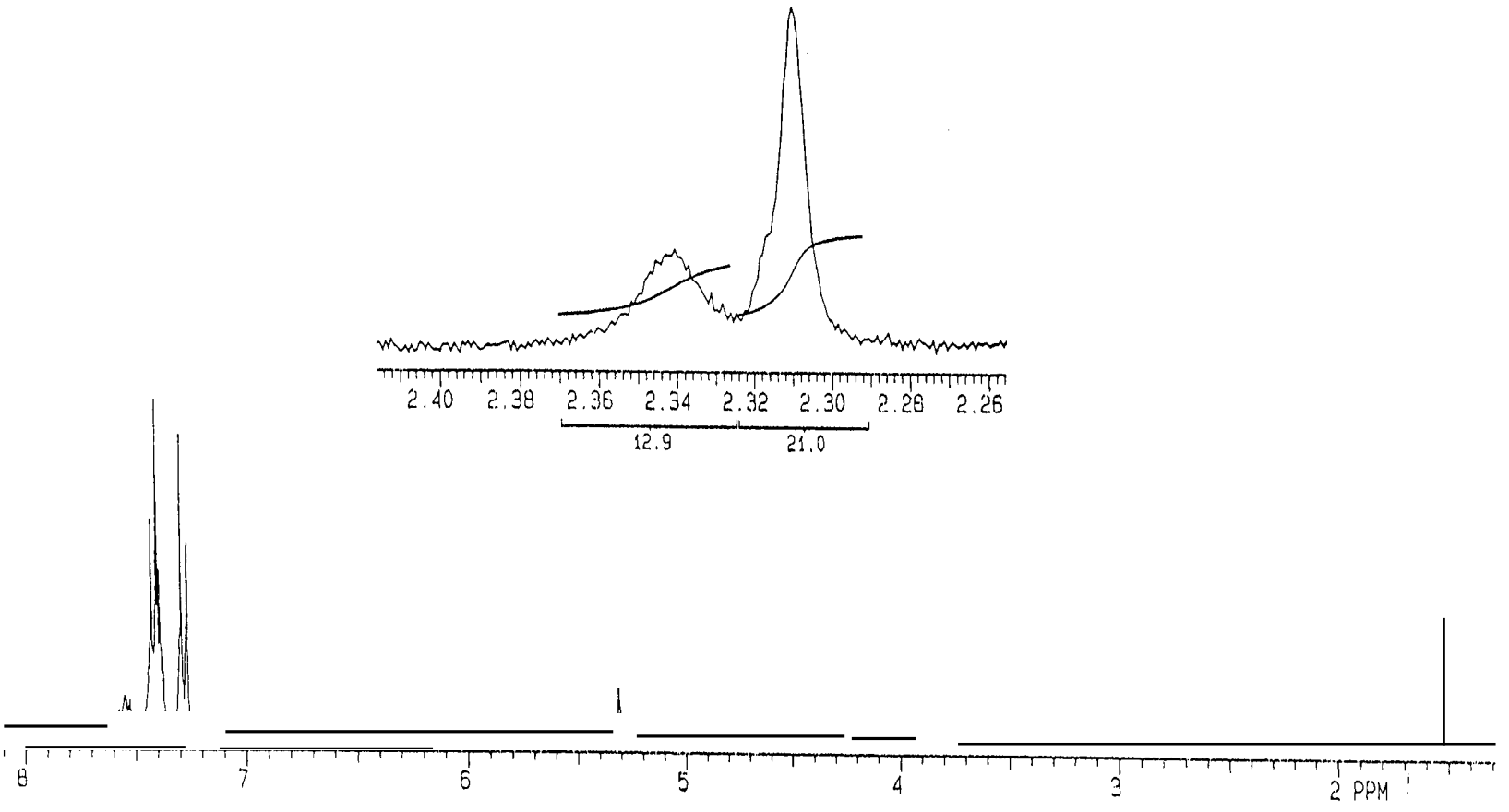


Figure 3.2. ^{1}H NMR of 1.94 mM $[(Ph_3PAu)_4(SC_6H_4CH_3)_3][PF_6]_2$ with 40 mM $ClC_6H_4SSC_6H_4CH_3$ after 1 hour in CD_2Cl_2

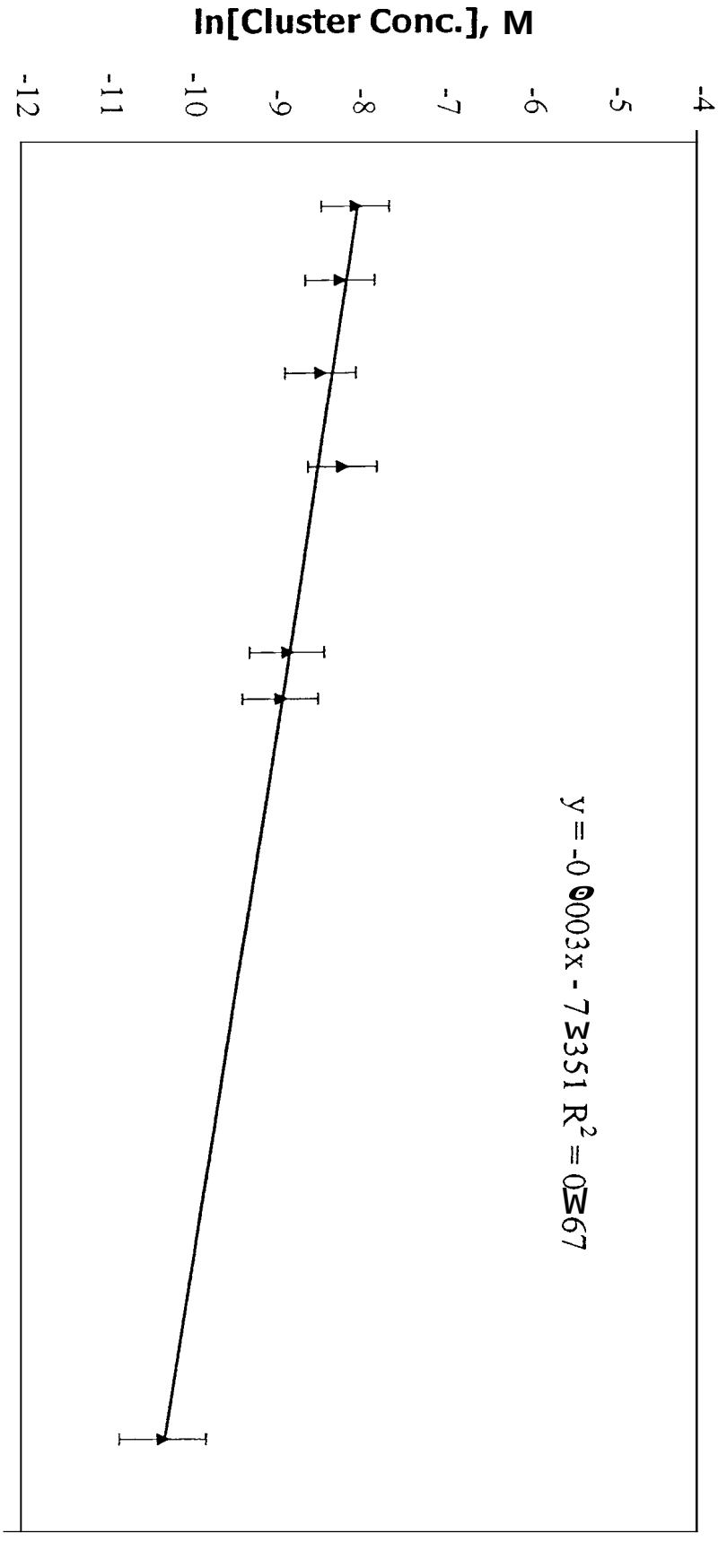


Figure 3.3. Run **A-1** ln conc. of $[(Ph_3PAu)_4(SC_6H_4CH_3)_2](PF_6)_2$, M vs. Time (sec)

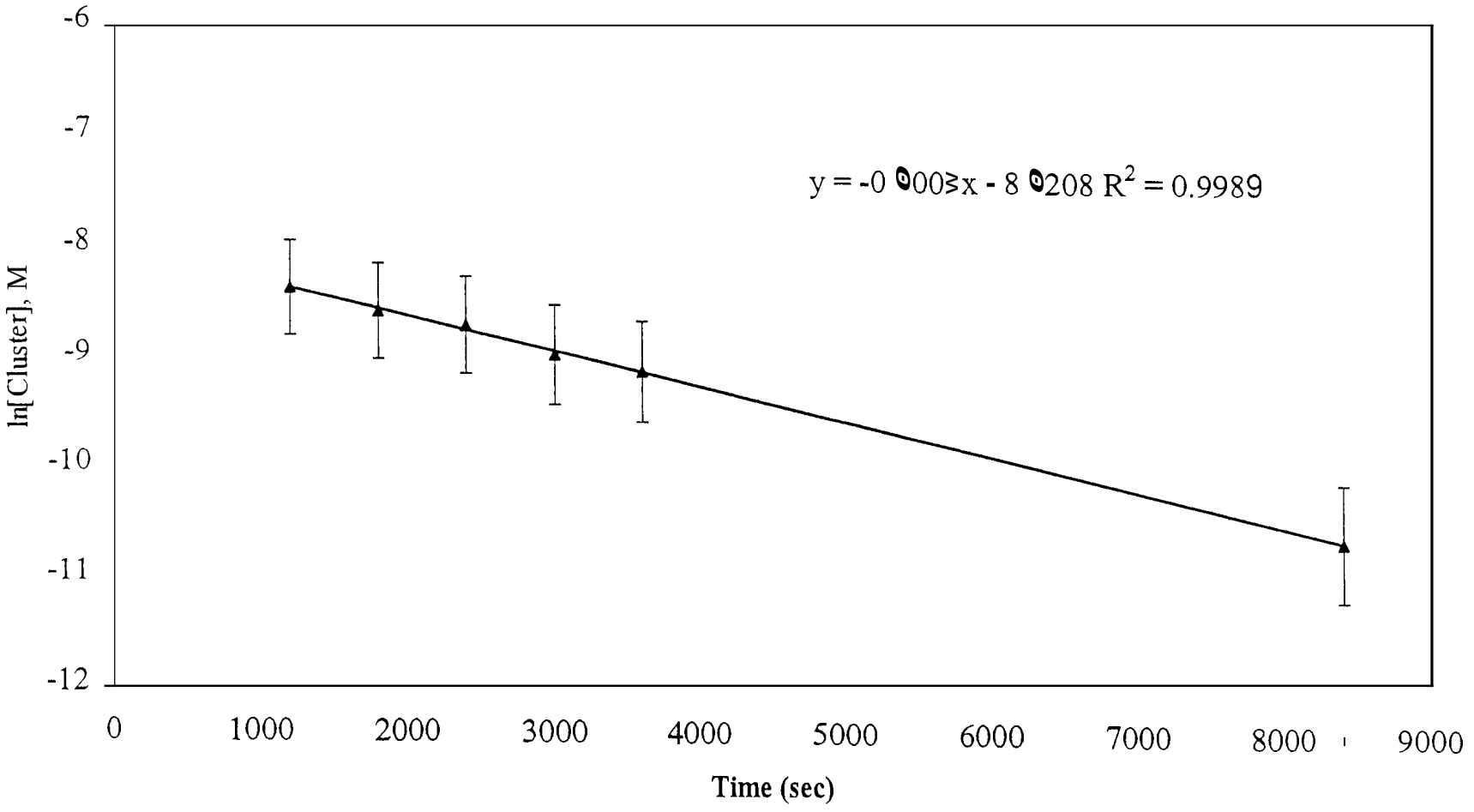


Figure 3.4. Run **A-2** ln conc. of $[(Ph_3PAu)_4(SC_6H_4CH_3)2](PF_6)_2]$, M vs Time (sec).

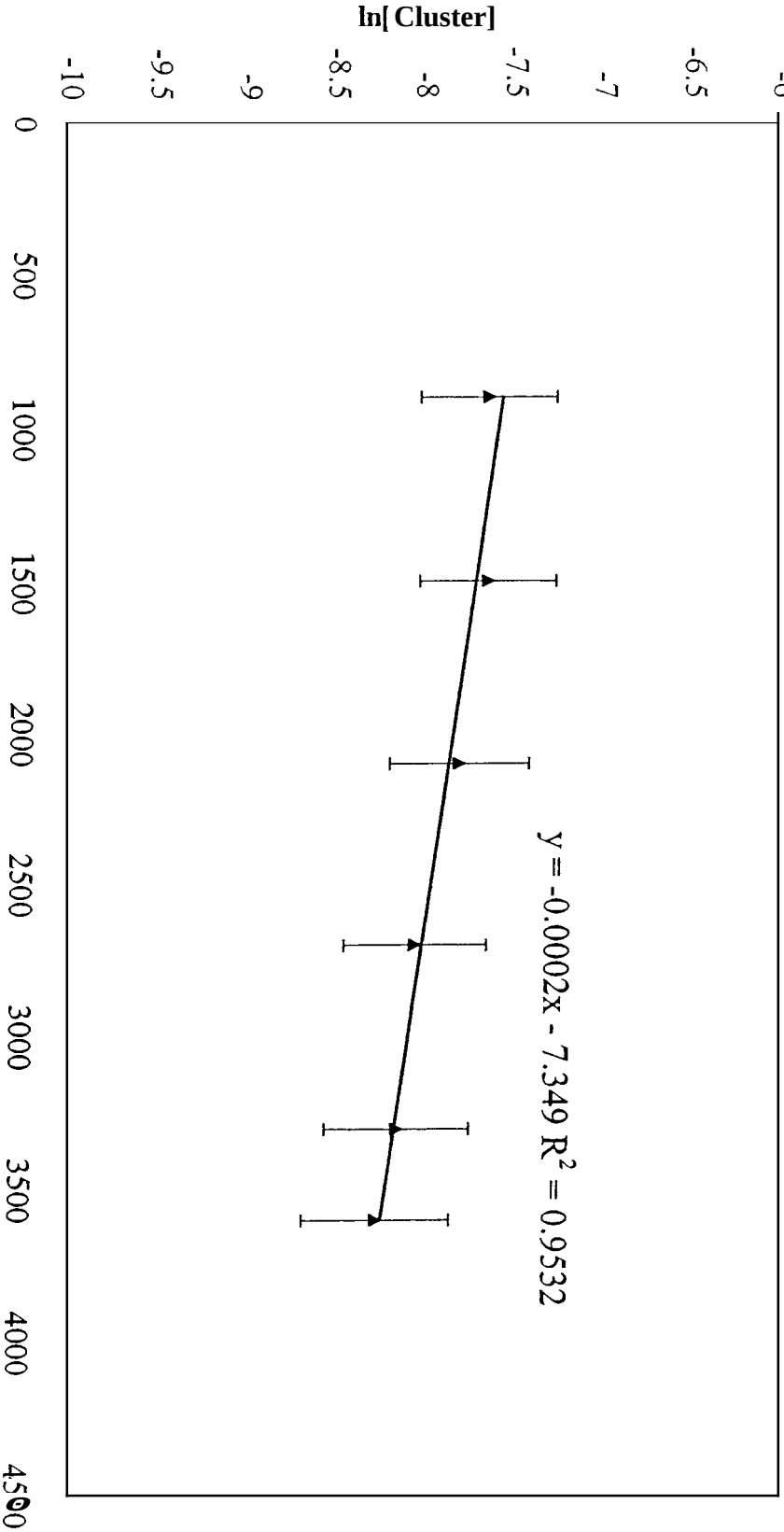


Figure 3.5. Run **B-1** ln conc. of $[(Ph_3PAu)_4(SC_6H_4CH_3)2](PF_6)_2$ vs. Time (sec).

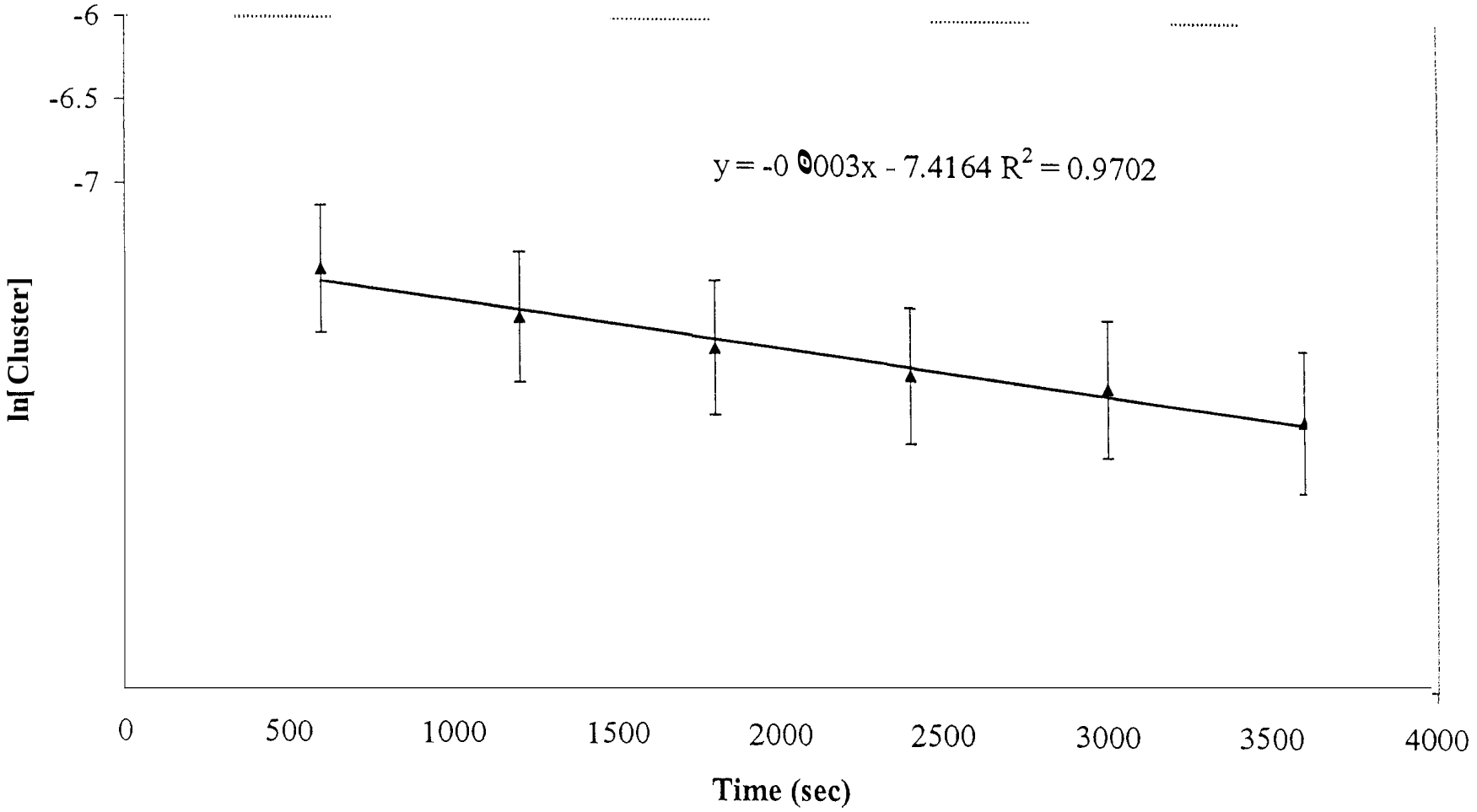


Figure 3.6. Run **B-2** ln conc. of $[(Ph_3PAu)_4(SC_6H_4CH_3)_2](PF_6)_2$ vs. Time (sec)

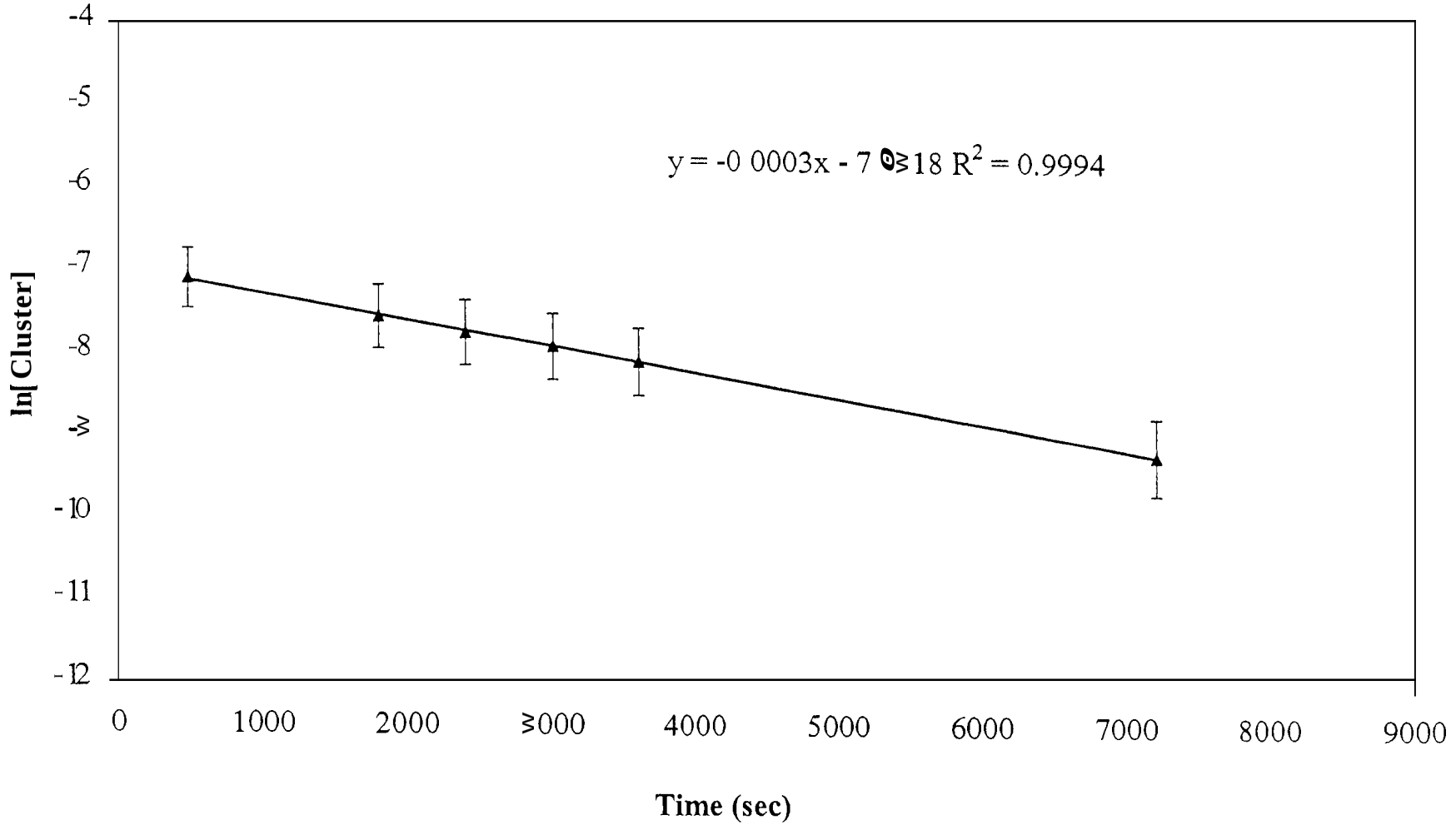


Figure 3.7. Run **C-1** ln conc. of $[(Ph_3PAu)_4(SC_6H_4CH_3)_2](PF_6)_2$ vs. Time(sec)

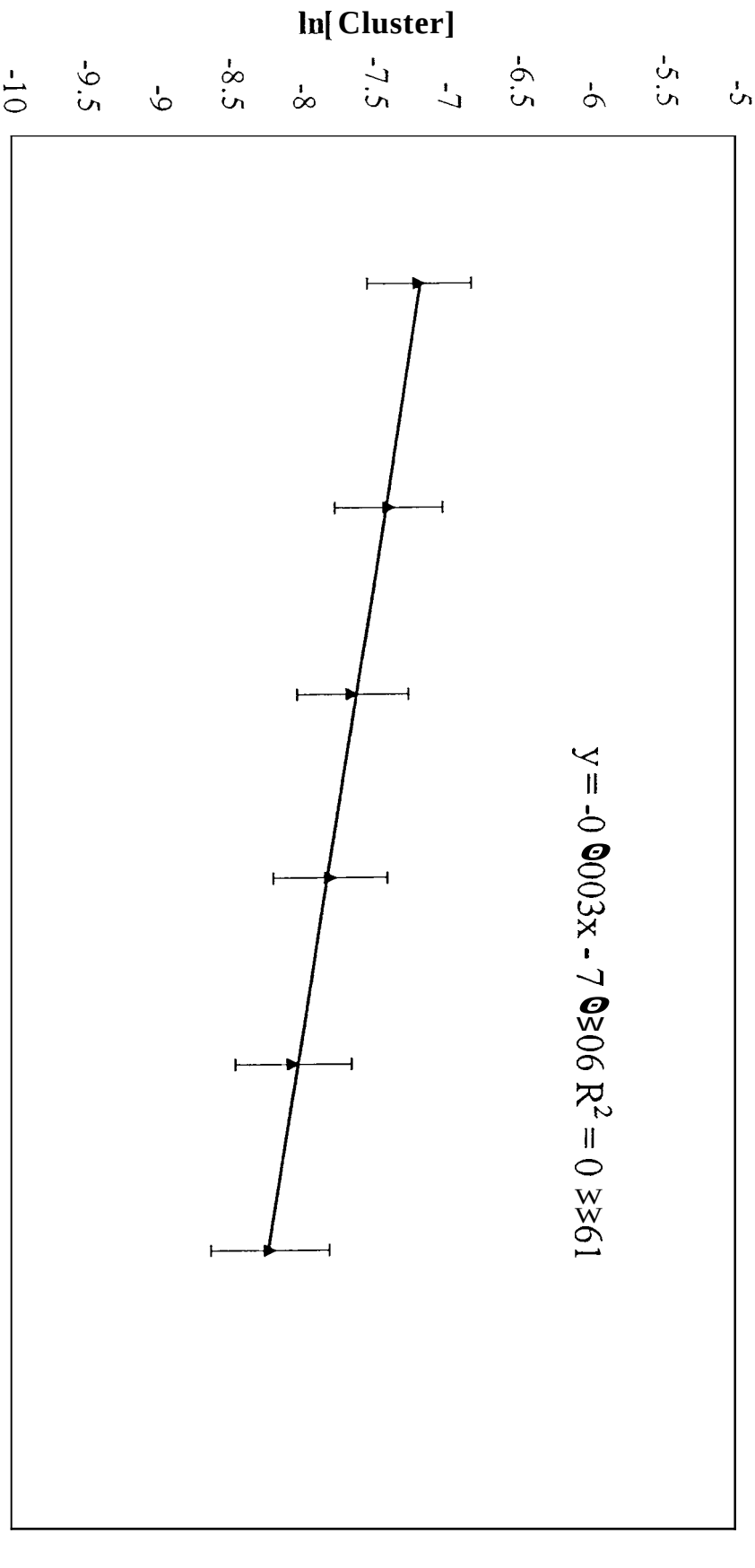


Figure 3.8. Run C-2 ln conc.of $[(Ph_3PAu)_4(SC_6H_4CH_3)_2](PF_6)_2$ vs. Time (sec)

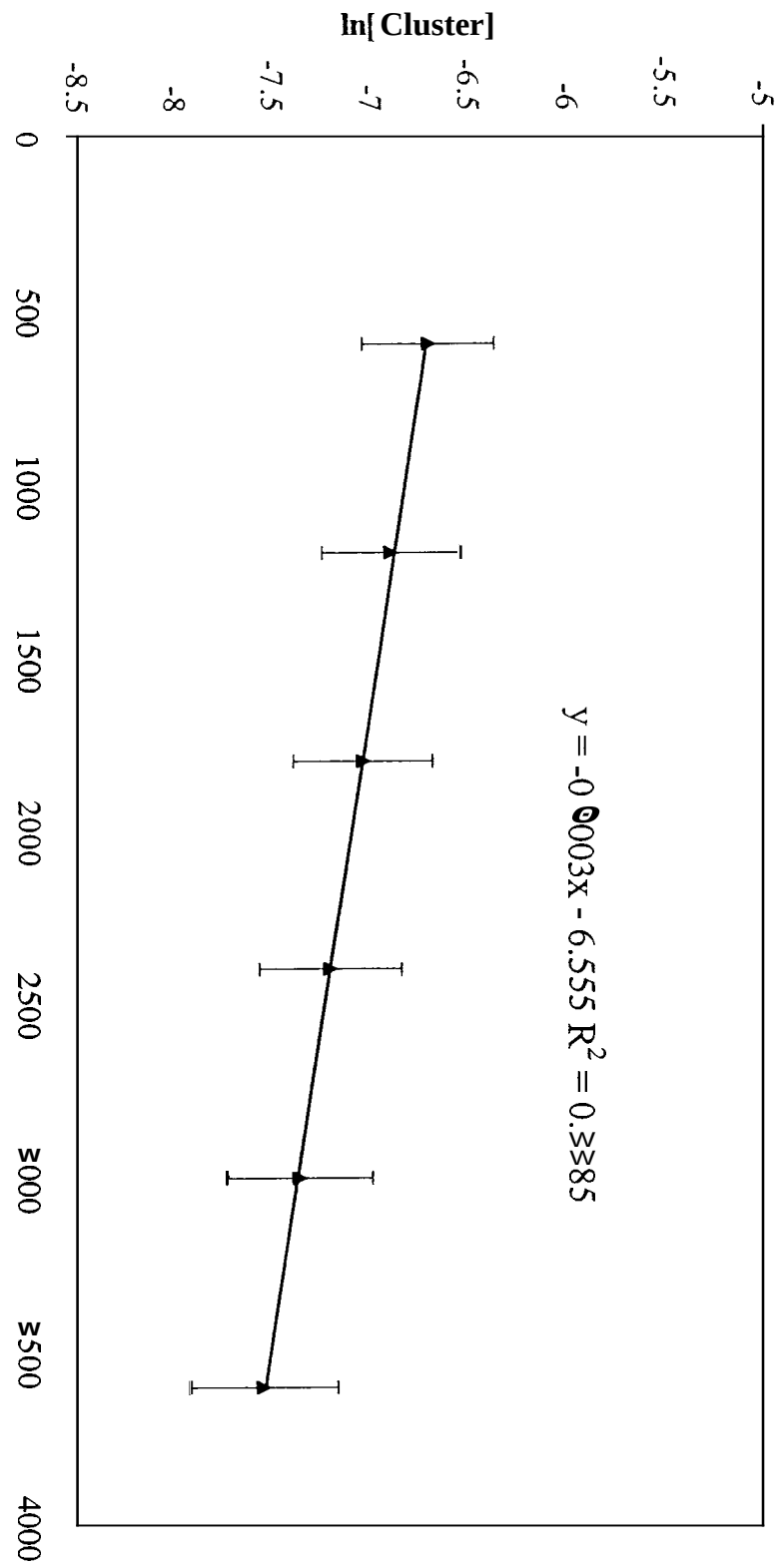


Figure 3.9. Run **D-1** ln conc. of $[(Ph_3PAu)_4(SC_6H_4CH_3)_2](PF6)_2$ vs. Time (sec)

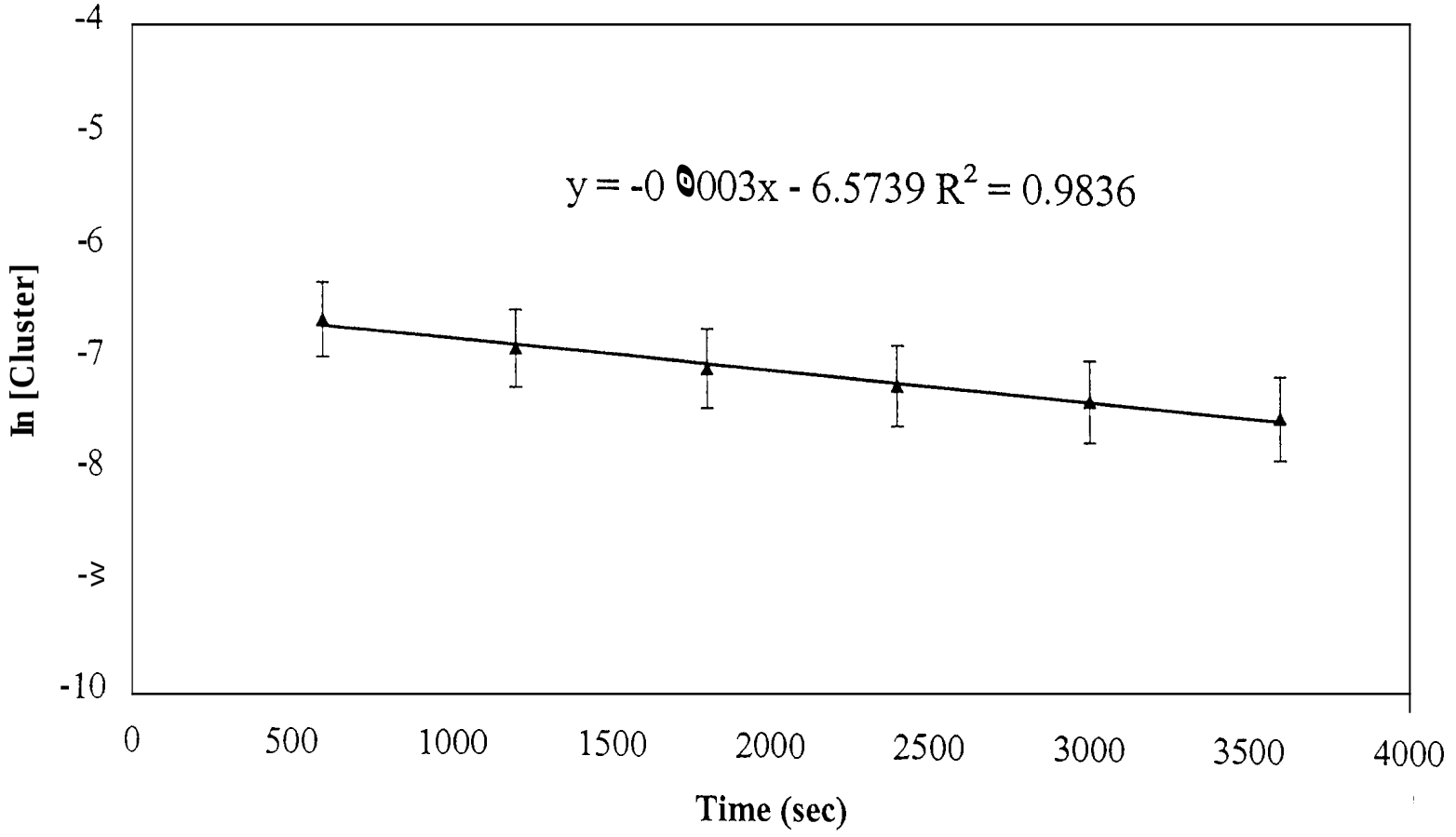


Figure 3.10. Run **D-2** conc. of $ln[(Ph_3PAu)_4(SC_6H_4CH_3)_2](PF_6)_2$ vs. Time (sec)

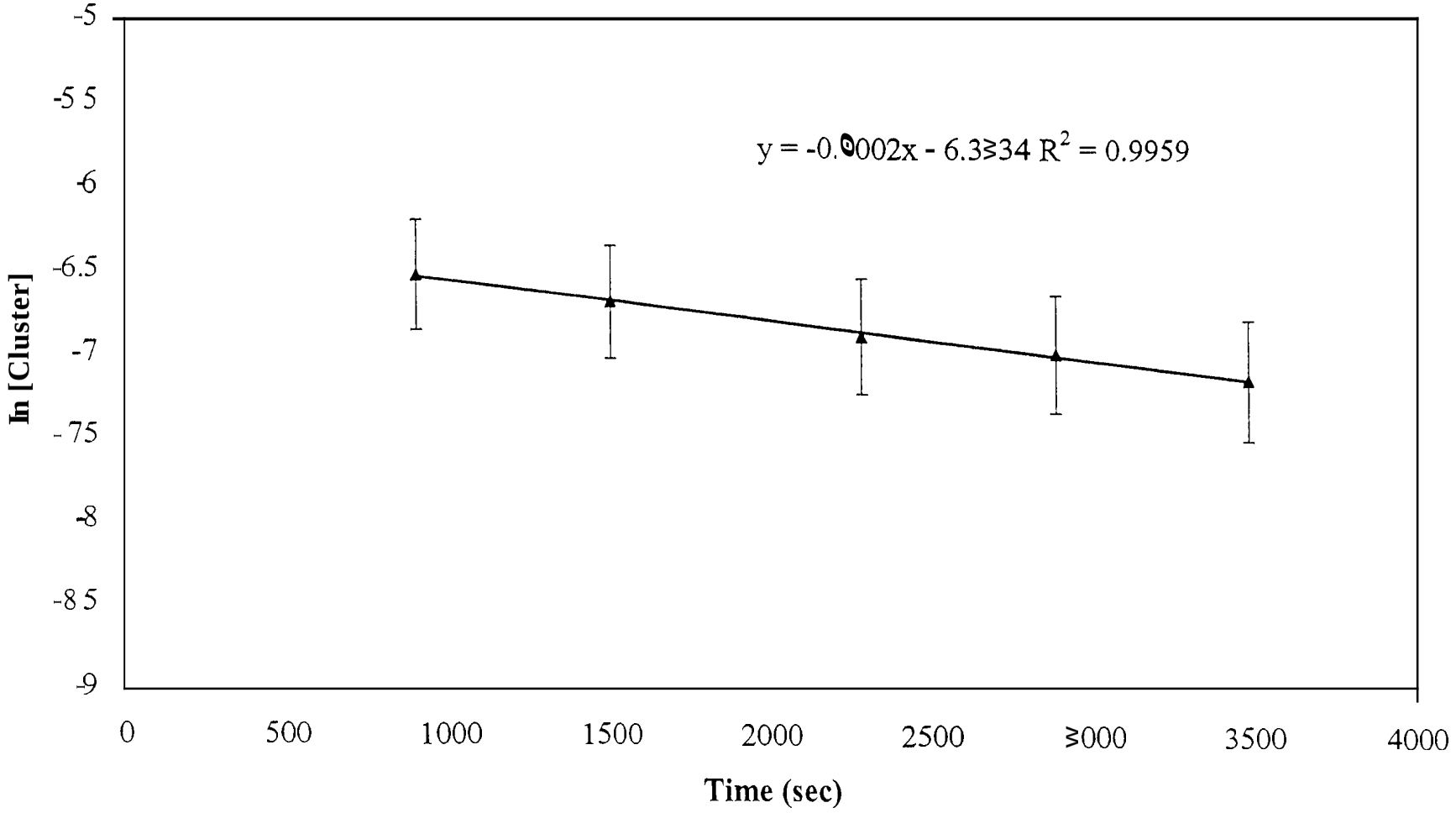


Figure 3.11. Run **E-1** ln conc. of$[(Ph_3PAu)_4(SC_6H_4CH_3)_2](PF_6)_2$ vs. Time (sec).

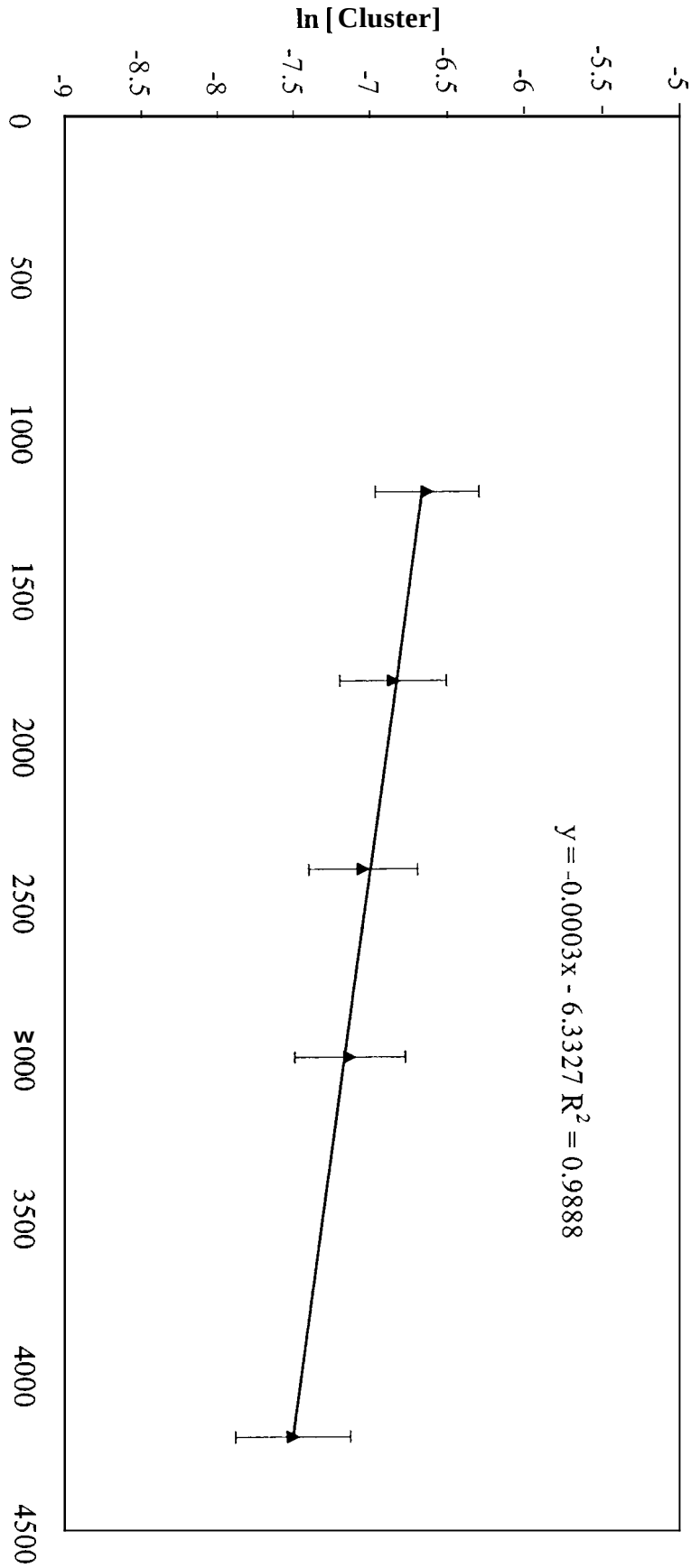


Figure 3.12. Run **E-2** ln conc. of $[(Ph_3PAu)_4(SC_6H_4CH_3)_2][PF_6]_2$ vs. Time (sec)

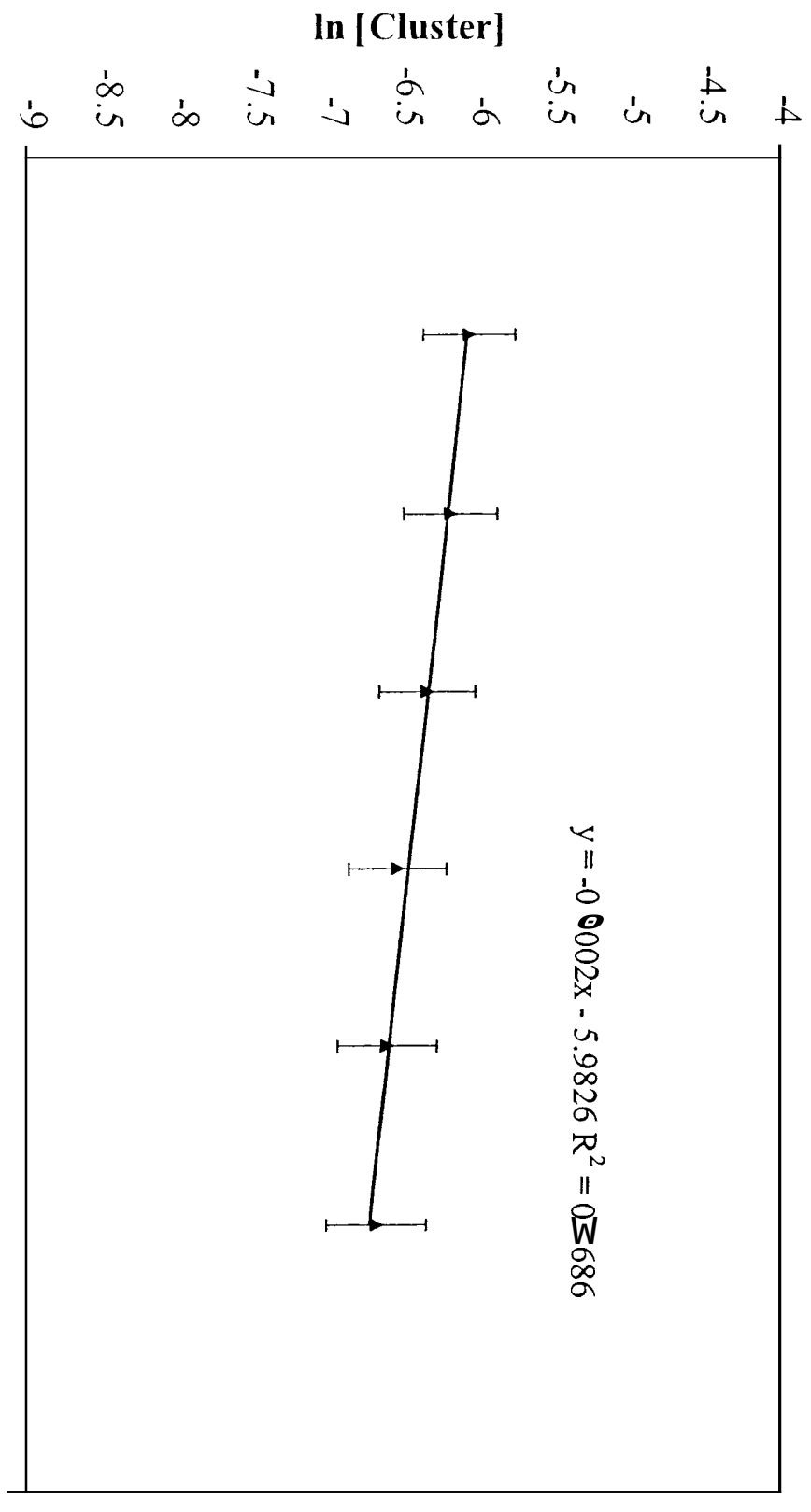


Figure 3.13. Run **F-1** ln conc. of $[(Ph_3PAu)_4(SC_6H_4CH_3)_2][PF_6]_2$ vs Time (sec)

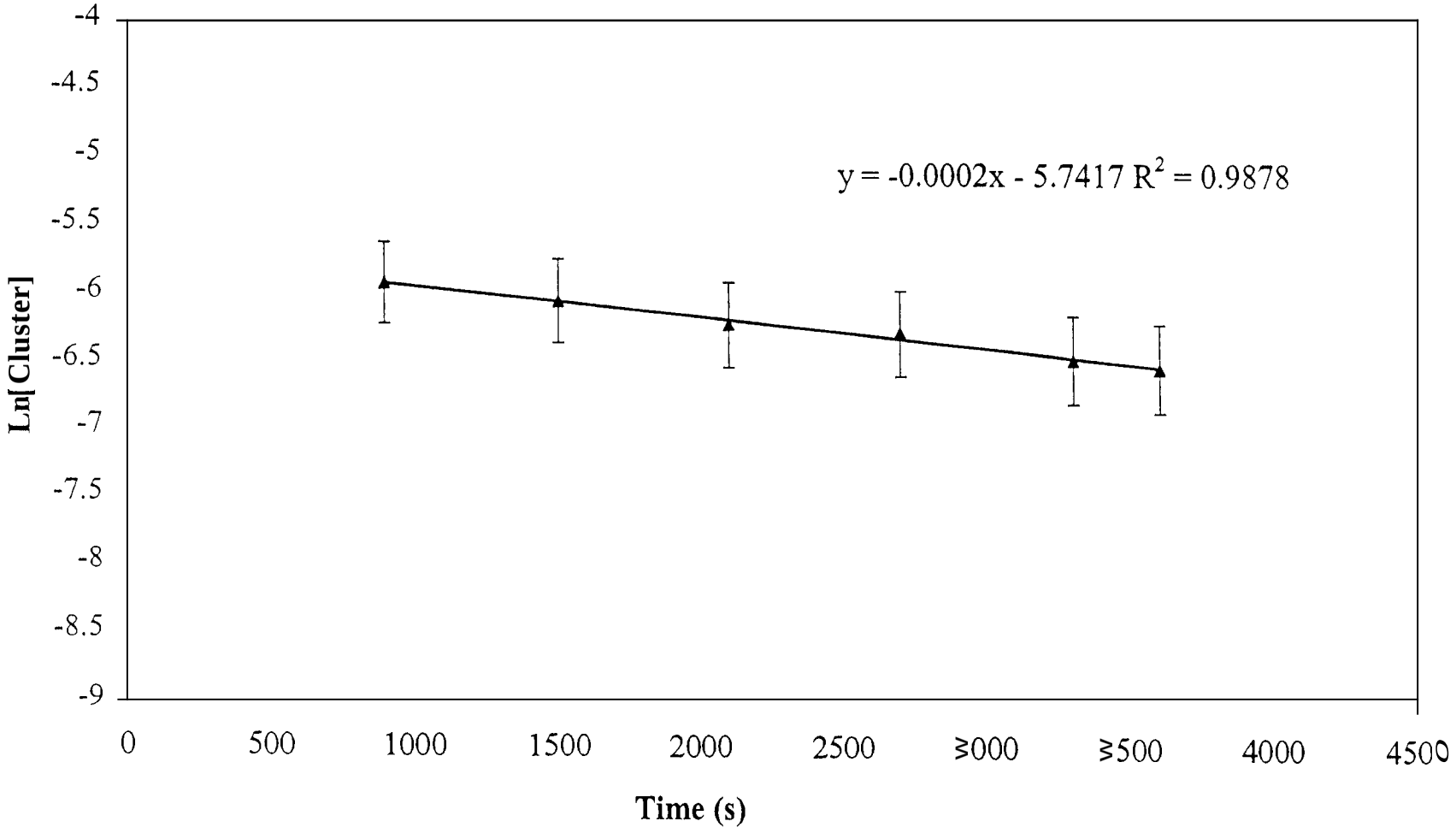


Figure 3.14. Run **F-2** ln conc. of$[(Ph_3PAu)_4(SC_6H_4CH_3)_2][PF_6]_2$ vs. Time (sec)

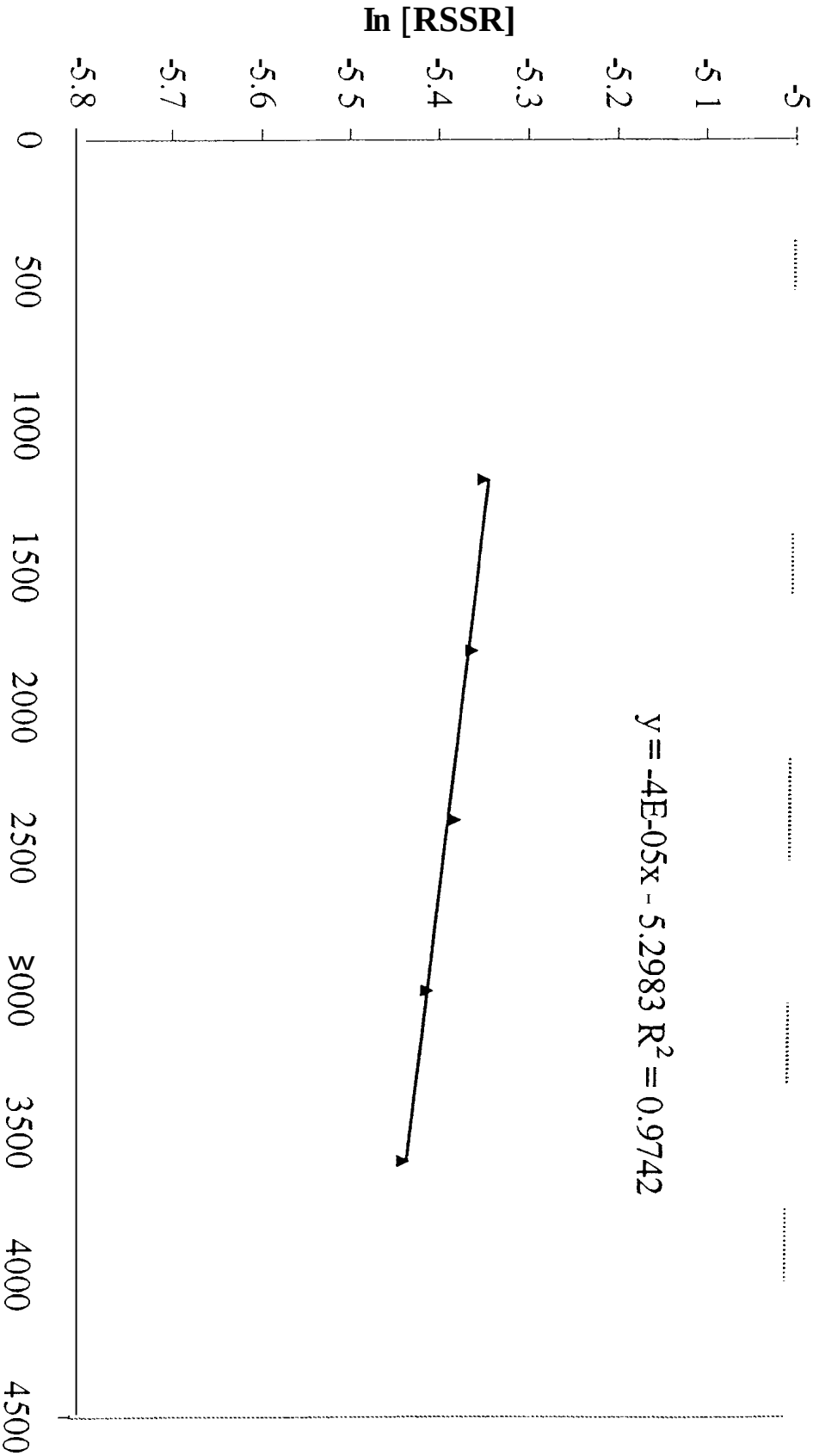


Figure 3.15. Run **G** ln [$ClC_6H_4SSC_6H_4Cl$] vs. Time (sec).

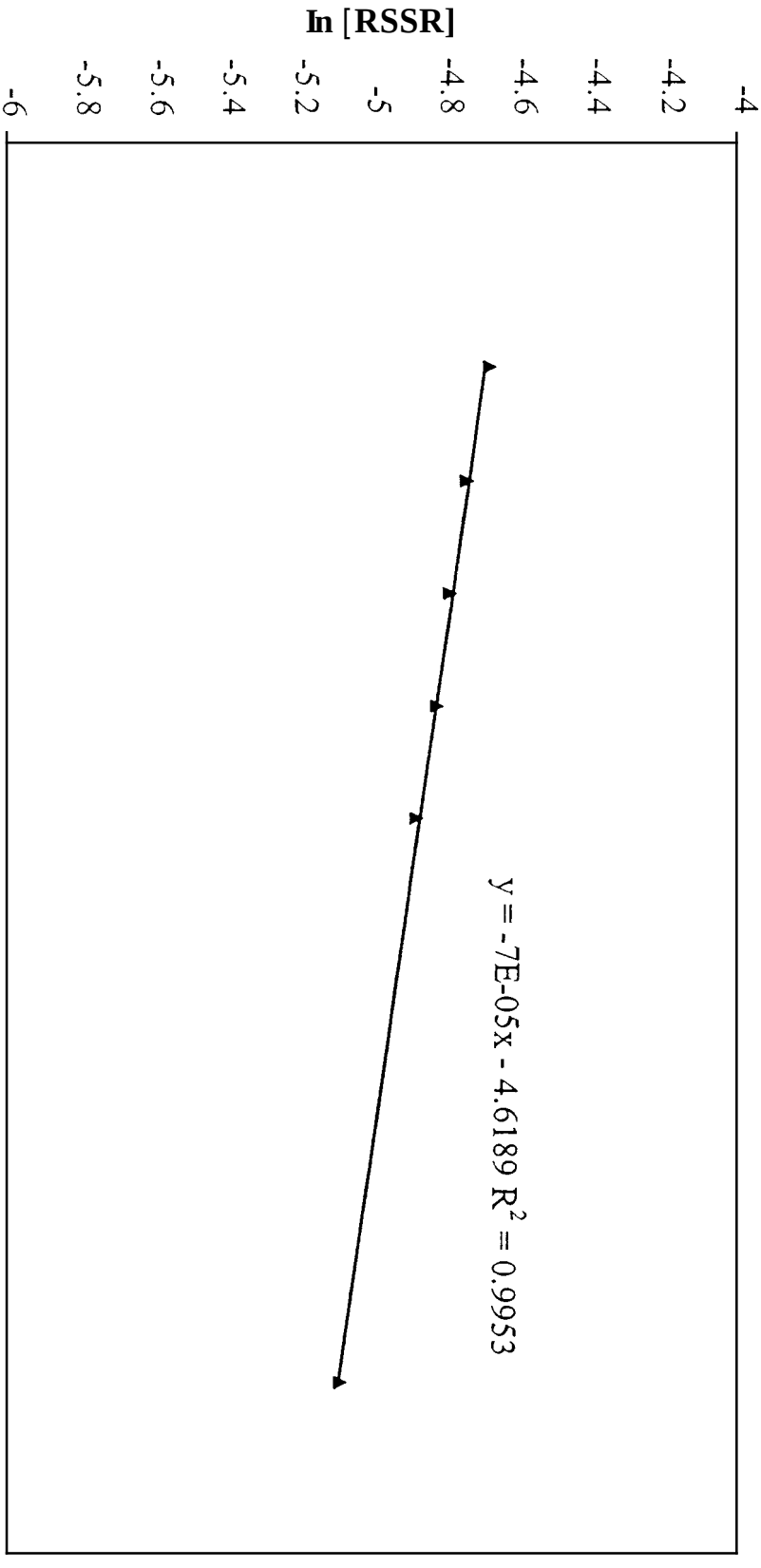


Figure 3.16. Run **H** ln [$ClC_6H_4SSC_6H_4Cl$] vs. Time(sec).

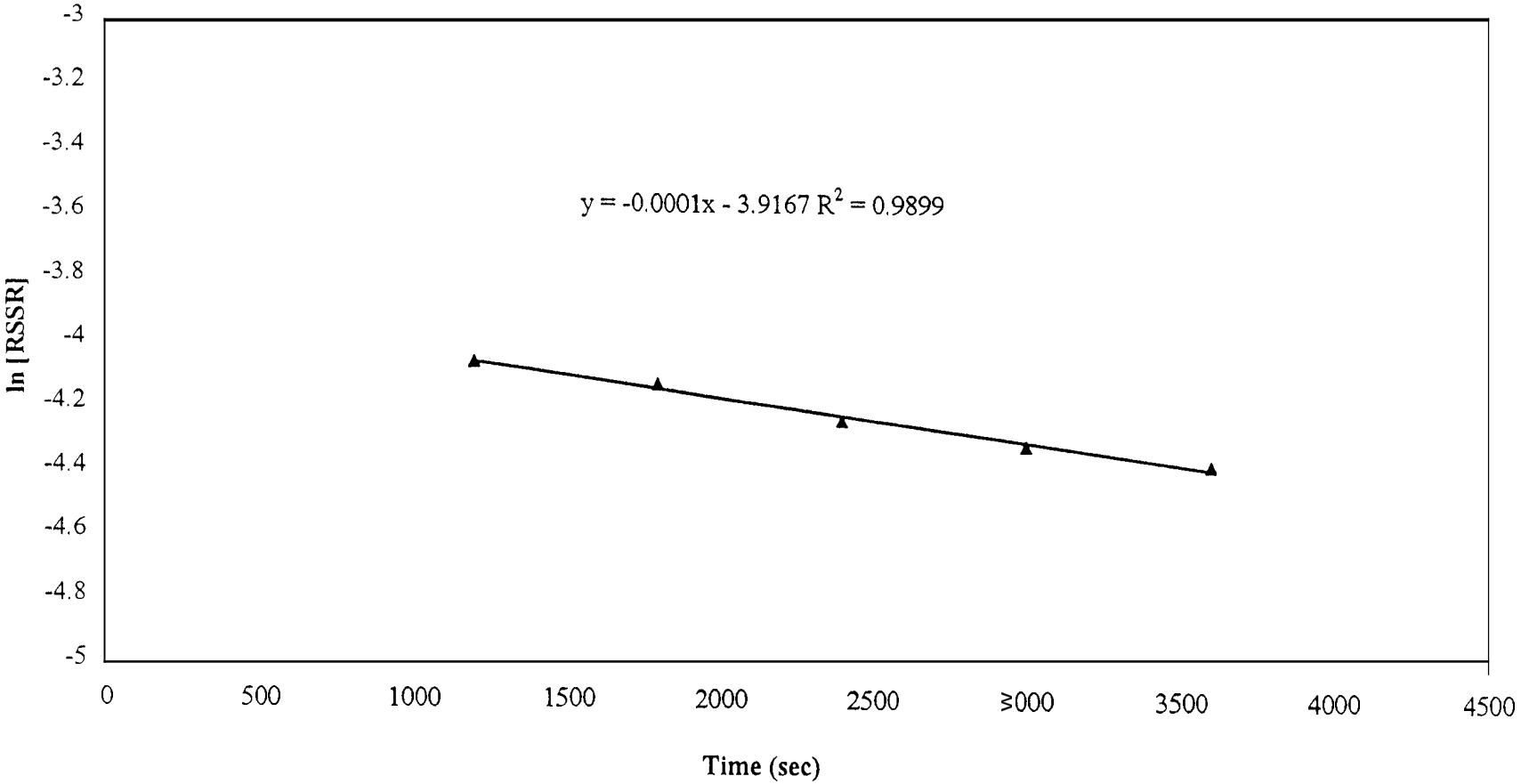


Figure 3.17. Run I ln $[ClC_6H_4SSC_6H_4Cl]$ vs. Time (sec)

However the rate constants, **k** (1.2 **x** 10^{-2}, 2.3 x 10^{-2} and **4.9** x 10^{-2}) may not be reliable since this set of experiments was not conducted under pseudo-first order conditions as described in the experimental part.

To summarize, the data are consistent with the rate law shown in Equation **3.5.**

$$\textbf{Rate} = k\,[(Ph_3PAu)_4(SC_6H_4CH_3)_2^{2+}][ClC_6H_4SSC_6H_4Cl] \qquad \textbf{3.5}$$

Comparison studies

(a) Determining the order of reaction in the neutral complexes: $Ph_3PAu(SC_6H_4CH_3)$, $[dppmAu_2(SC_6H_4CH_3)_2]$ and $[dppeAu_2(SC_6H_4CH_3)_2]$

These experiments were conducted under pseudo first order conditions. Thus the initial concentration for each neutral gold complex was 3.2 mM and the intial disulfide concentration was 40.0 mM (Run J-L). Each run was duplicated and the data for one of the J runs was thrown out due to inaccurate integrals as a result of improper shimming of the ***NMR.***

Figures **3.18-3.22** show plots of ln[complex] (M) versus time(s). These plots are also consistent with first order in the neutral gold complex concentration. The rate constants are shown in Table **3.5.** More experiments need to be done, i.e., varying the concentration as was done for the cluster kinetic experiments.

(b) Determining the order of reaction in $[(dppb)_2Au_4(SC_6H_4CH_3)_2][PF_6]_2$

These experiments were done under pseudo first order conditions. The initial concentration of cluster varied from 1.16-3.10 mM and the initial disulfide concentration

was held constant at 40.0mM (run M-O). Figures **3.23-3.25** show plots of [cluster] (M) versus time(s) and also are consistent with first order in cluster concentration. The rate constants are shown in Table **3.5.**

Table 3.5. The rate constants of the gold(I) complexes.

Gold complexes	Slope (k_{obs})	Rate constant, k (M^{-1} sec^{-1})*	# of experiments
$[(Ph_3PAu)_4(SC_6H_4CH_3)_2][PF_6]_2$	-2.7×10^{-4}	$6.8 \pm 1.0 \times 10^{-3}$	12
$[(dppb)_2Au_4(SC_6H_4CH_3)_2][PF_6]_2$	-3.0×10^{-4}	7.5×10^{-3}	3
$[dppmAu_2(SC_6H_4CH_3)_2]$	-5.7×10^{-5}	1.4×10^{-3}	2
$[dppeAu_2(SC_6H_4CH_3)_2]$	-9.8×10^{-6}	2.4×10^{-4}	2
$Ph_3PAu(SC_6H_4CH_3)$	-1.3×10^{-5}	3.4×10^{-4}	1

Equation **3.4.**

The comparison studies can be summarized by the qualitative ordering as follows:

$$[(dppb)_2Au_4(SC_6H_4CH_3)_2][PF_6]_2 \geq [(Ph_3PAu)_4(SC_6H_4CH_3)_2][PF_6]_2 >$$

$$[dppmAu_2(SC_6H_4CH_3)_2] > Ph_3PAu(SC_6H_4CH_3) > [dppeAu_2(SC_6H_4CH_3)_2]$$

Thus the cluster complexes which have 4 Au-Au interactions react faster than the dinuclear complex, $[dppmAu_2(SC_6H_4CH_3)_2]$ which exists in solution as 2 conformers, one of which has a Au-Au bond.[6] The slowest rates were observed for the complexes which do not contain a Au-Au bond. Another factor which may play an important role is the charge. The cluster complexes are cationic and there is conductivity data that supports the fact that $[dppmAu_2(SC_6H_4CH_3)_2]$ is a weak electrolyte in solution.[2]

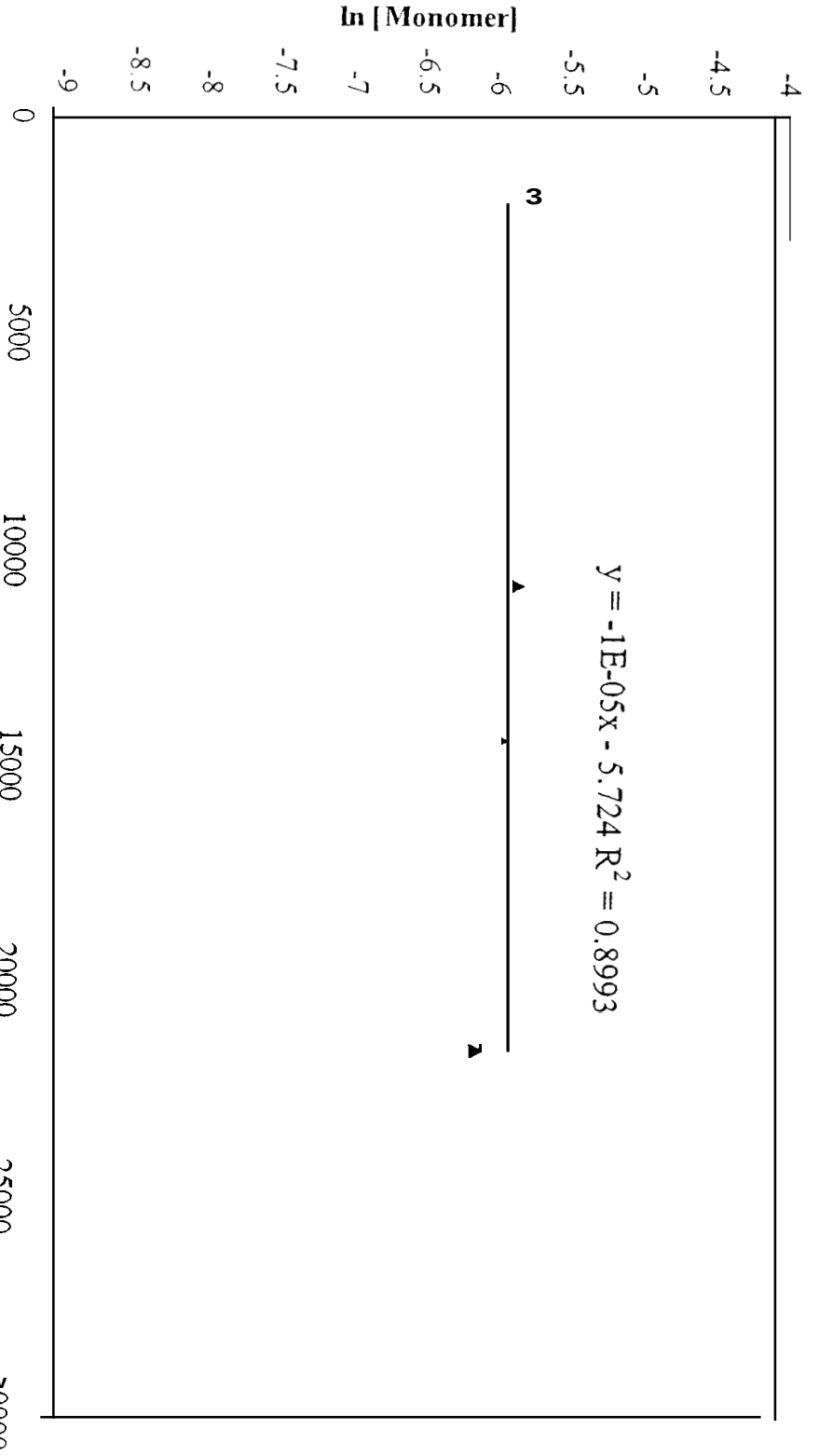


Figure 3.18. Run **J** ln [$Ph_3PAu(SC_6H_4CH_3)$] vs. Time (sec)

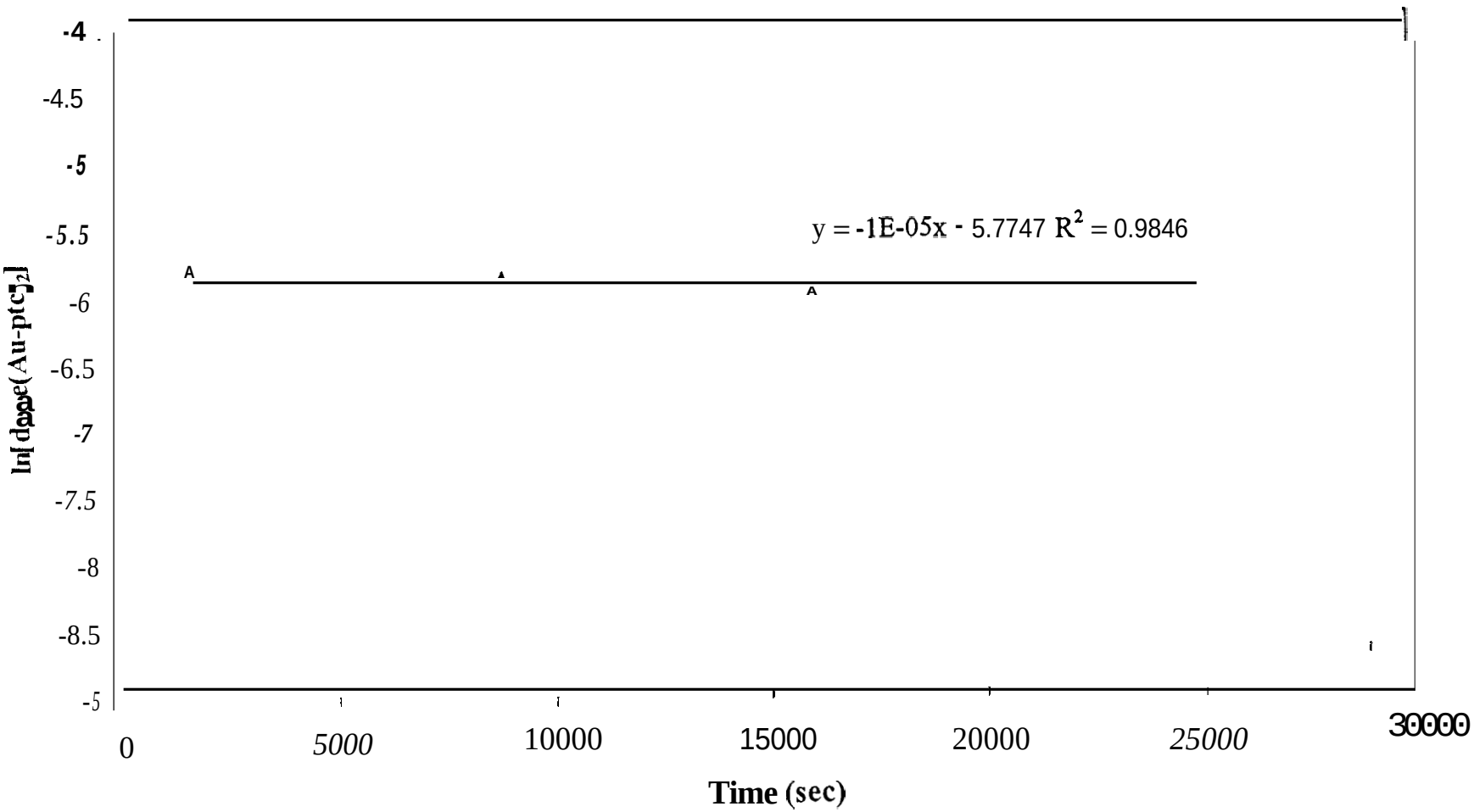


Figure 3.19. Run **K1** ln [dppe(Auptc)$_2$] vs Time(sec)

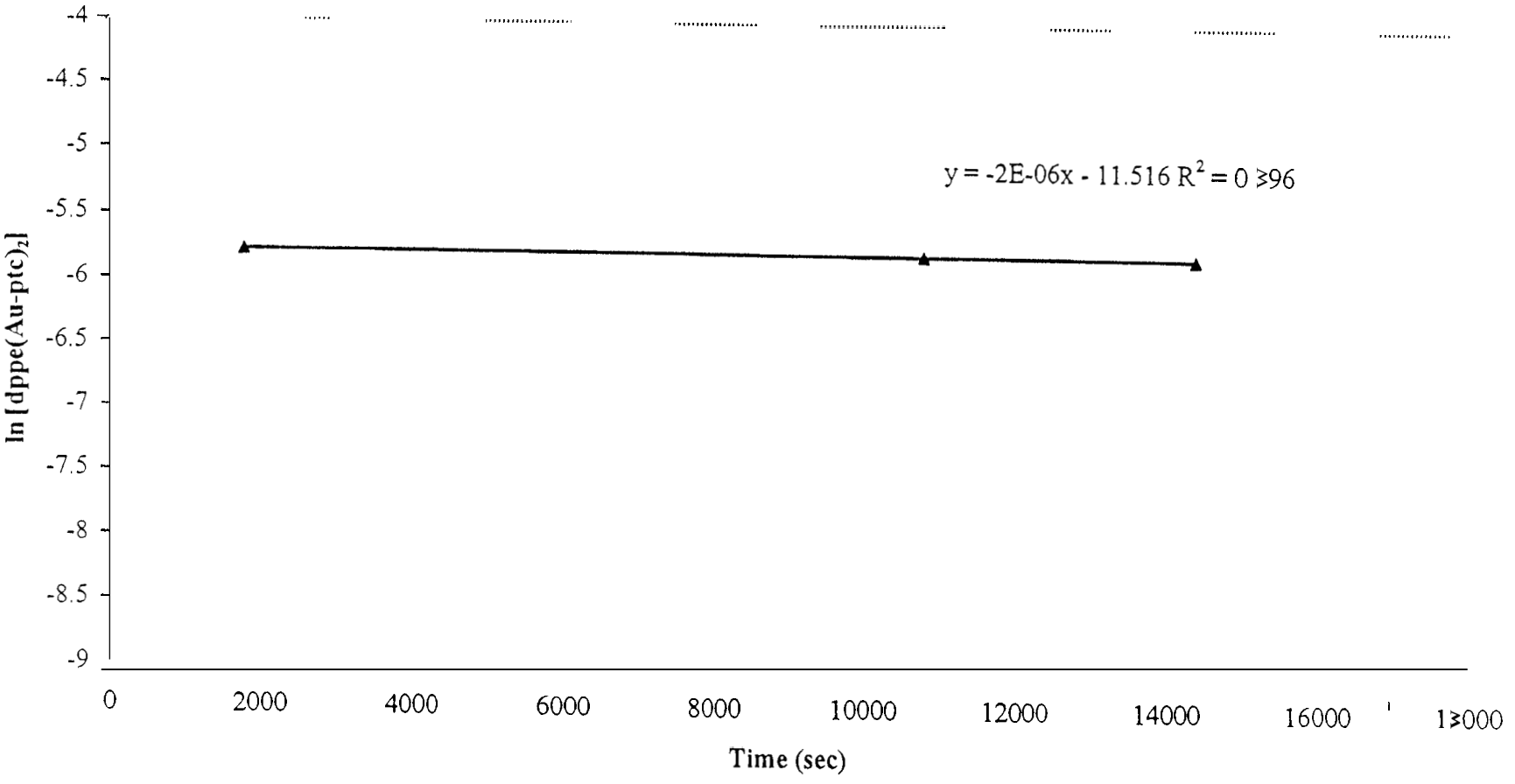


Figure 3.20. Run **K2** ln [dppe(Au-pt) $_2$] vs. Time [sec)

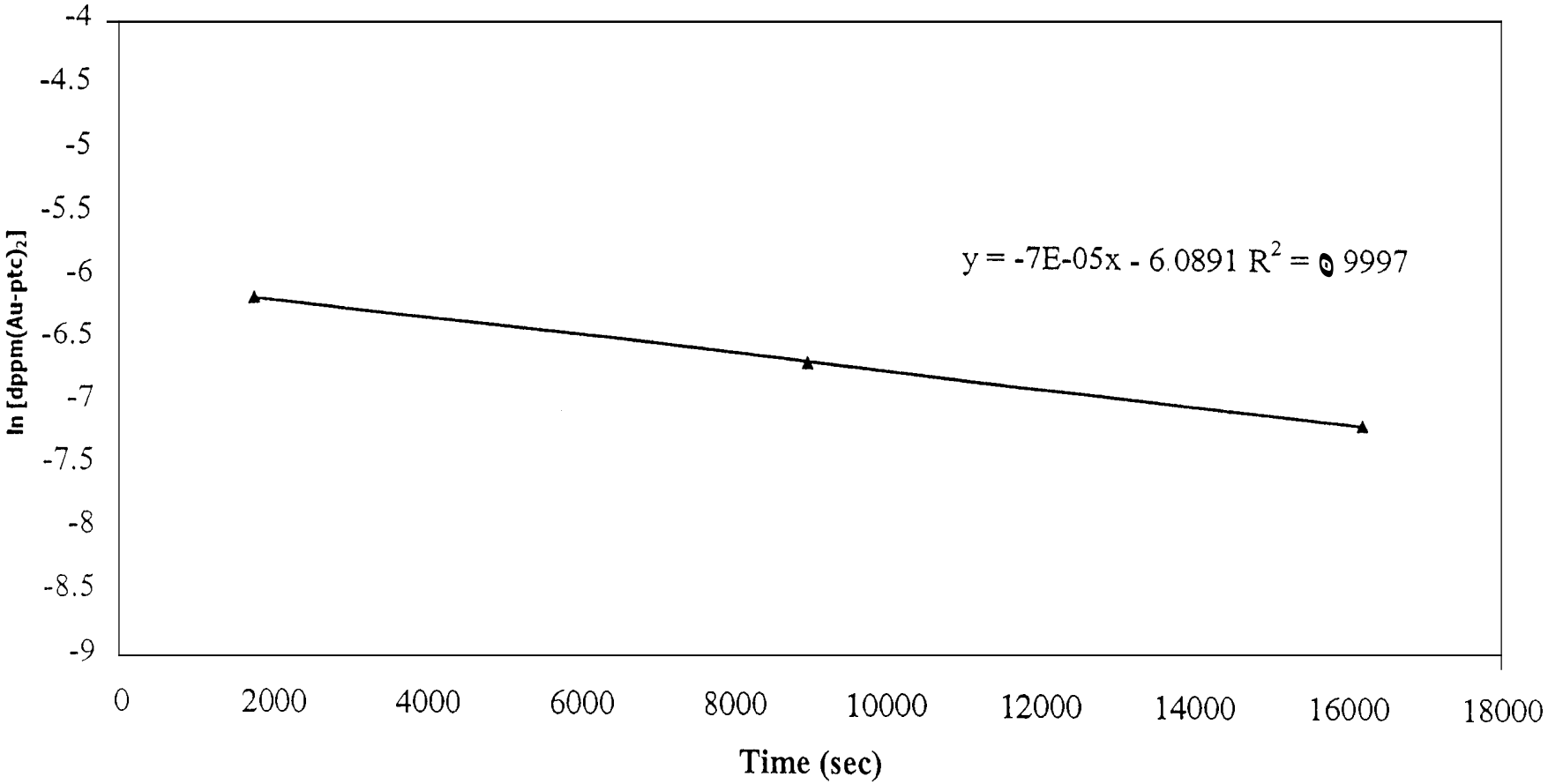


Figure 3.21. Run **L1** ln [dppm(Au-ptc)$_2$] vs. Time (sec)

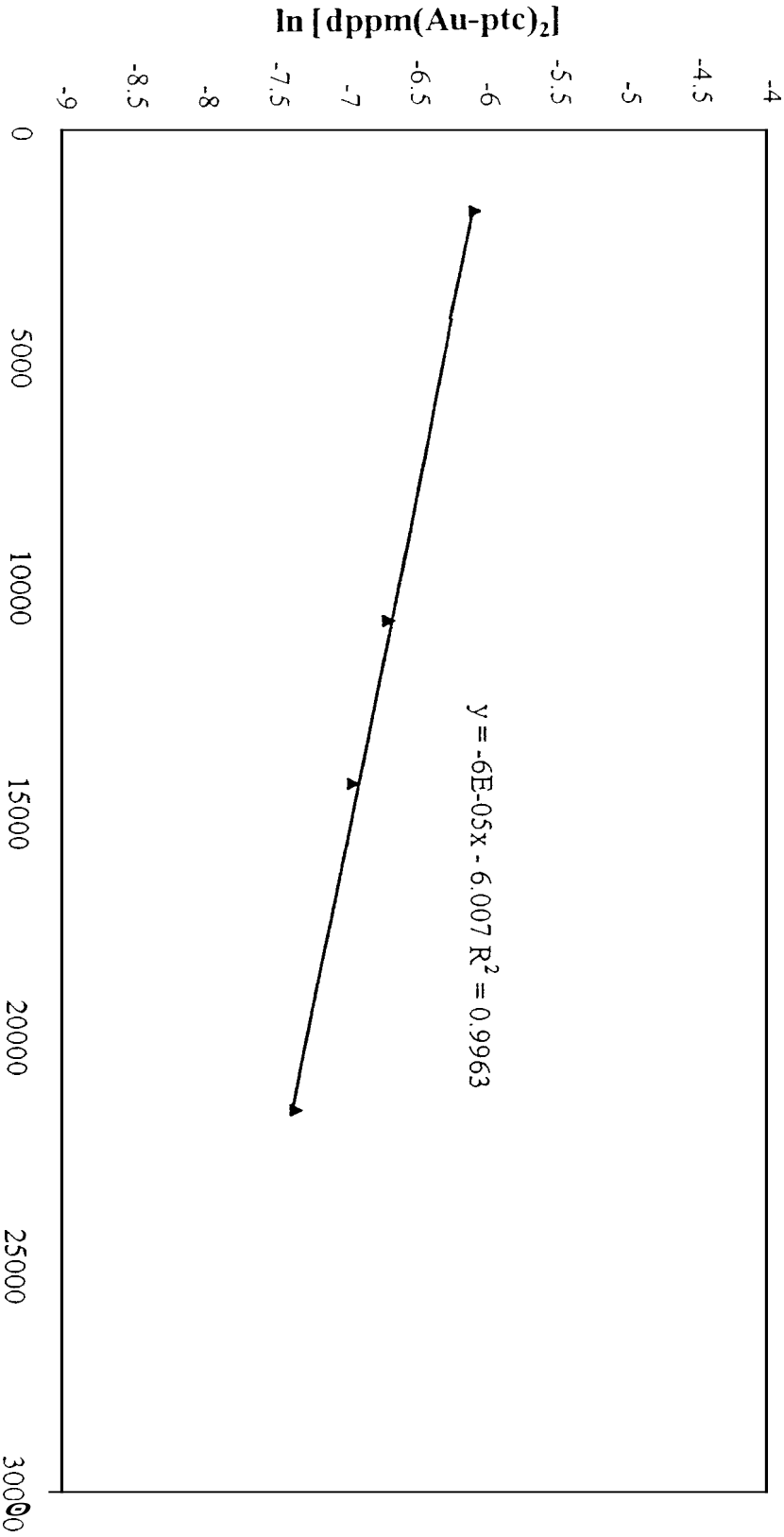


Figure 3.22. Run **L2** ln [dppm(Au-ptc)$_2$] vs Time (sec).

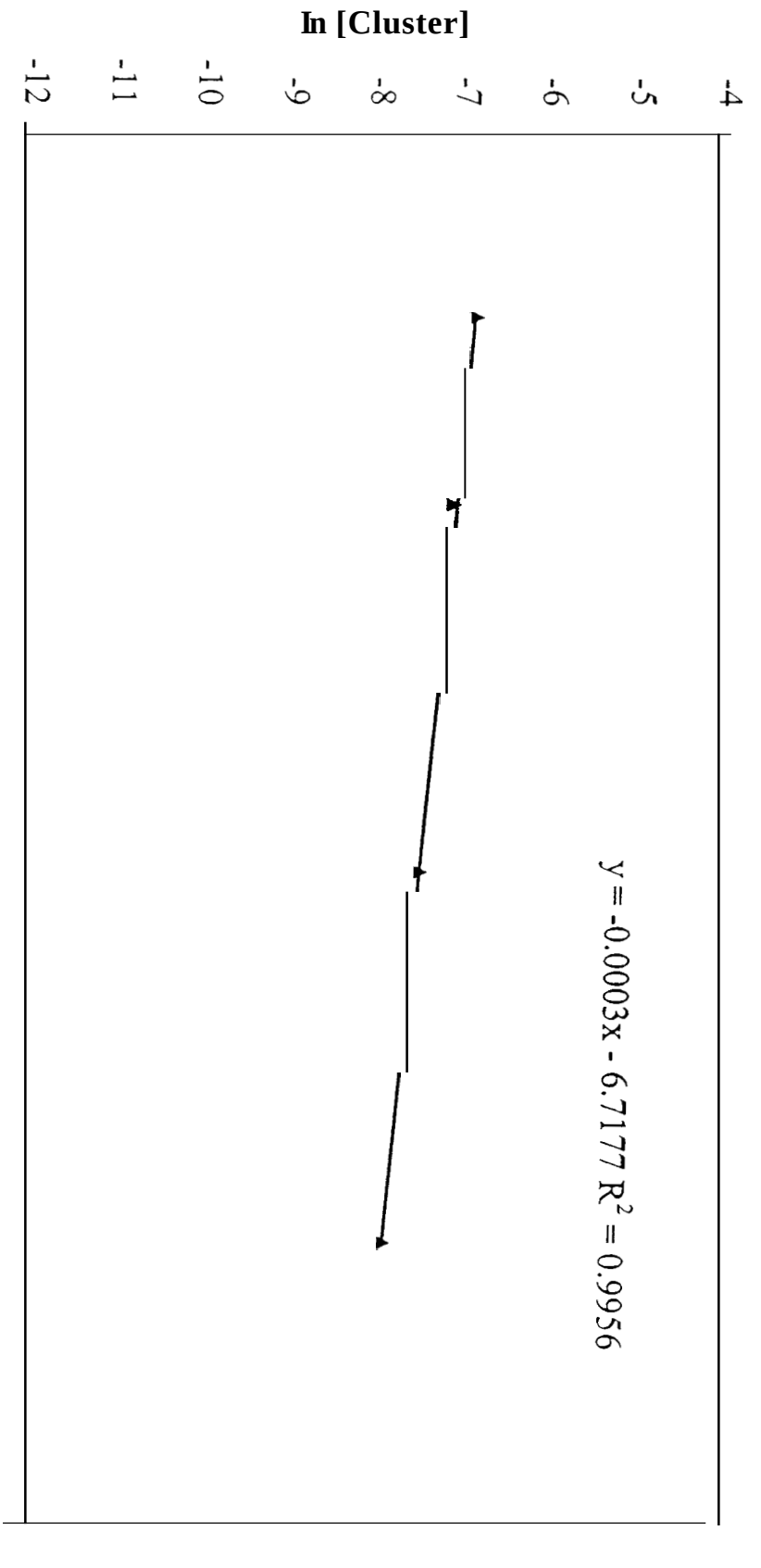
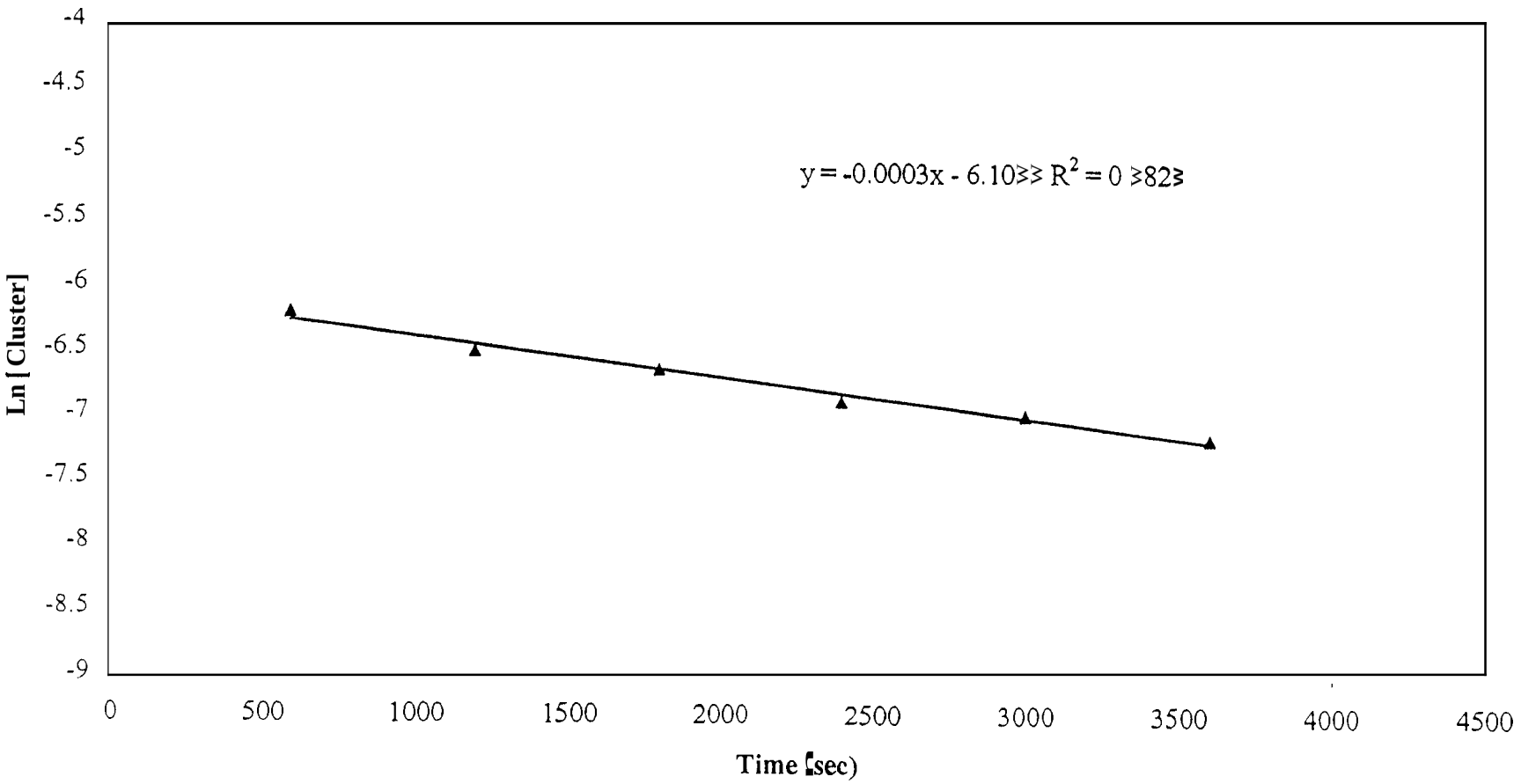


Figure 3.23. Run **M** ln conc. of $[(dppb)_2Au_4(SC_6H_4CH_3)_2](PF_6)_2$ vs. Time (sec).



Fj ure 3.24. Run N ln conc. of $[(ppb)_2Au_4(SC_6H_4CH_3)_2](PF_6)_2$ vs. Time (sec)

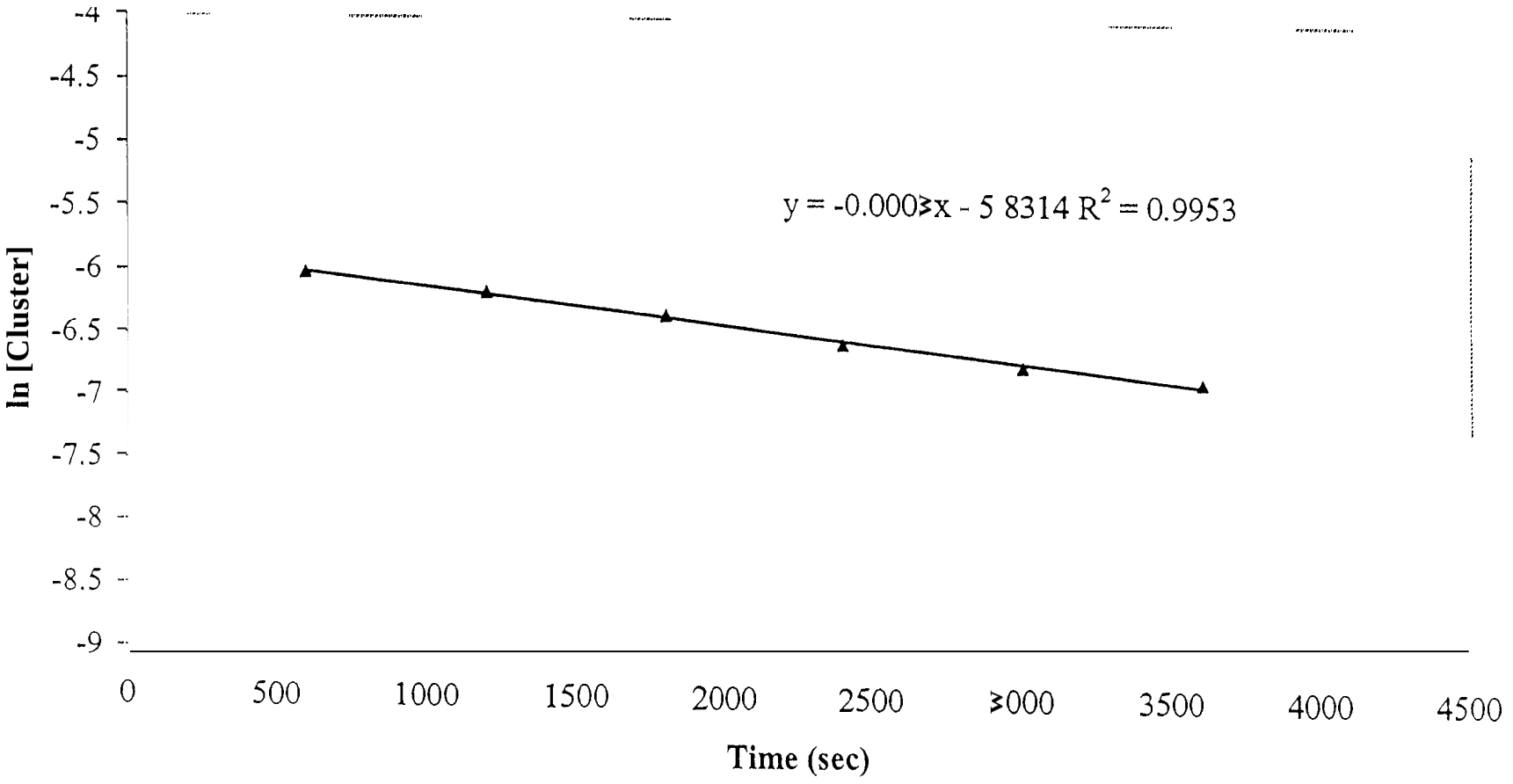


Figure 3.25. Run O ln oonc. of $[(dppb)_2Au_4(SC_6H_4CH_3)_2](PF_6)_2$ vs. Time (seo)

References

1. Ganesh, **S.** Master Thesis. University of Maine, **1995**.

2. Dilorenzo, M. Master Thesis. University of Maine, 1997.

3. Chen, J. M. Sc. thesis. University of Maine, 1999.

4. Dilorenzo, M.; Ganesh, S.; Tadayon, L.; Bruce, M. R. M.; Bruce, **A.** E *Metal-Based Drugs,* 1999, 6,247.

5. Chen, J.; Jiang, T.; Wei, G.; Mohamed, **A. A.;** Homrighausen, C.; Bauer, J. **A.,** Bruce, **A.** E.; Bruce, M. R. M. *J. Am. Chem. Soc.* 1999,121,9225-9226.

6. Narayanasaswamy, R.; Young, M. **A.;** Parkhurst, E.; Ouellette, M.; Kerr, M. E.; Ho. D.; Elder, R. C.; Bruce, **A.** E.; Bruce, M. R. M. *Inorg. Chem.*, 1993, 32, 2506-2517.

BIBLIOGRAPHY

1. Bachmann, B.; Hahn, F; Heck, J.; Wunsch, M. *Organometallics*, **1989**, *8*, 2523.

2. Bardaji, M.; Connelly, N. G.; Gimeno, M. C.; Jones, P. J.; Laguna, **A.;** Laguna, M., *J.Chem. Soc., Dalton Trans.*, **1995,2245.**

3. Berners-Price, **S.** J.; Sadler, P. J. in *Frontiers in Bioinorganic Chemistry*, Xavier, **A.** V., Ed., VCH, Weinheim, Germany, **1986, 376-388.**

4. Berners-Price, **S.** J.; Sadler, P. J. *Structure and Bonding*, **1988,** *70*, 27-102.

5. Bianchini, **C.;** Laschi, F.; Masi, D.; Ottaviani, F. M.; Pastor, **A.;** Peruzzini, M.; Zanobini, F. *J. Am. Chem. Soc.*, **1993,115,2723.**

6. Brown, D. H.; Smith, W. E. *Chem. Soc. Rev.*, **1980, 9,217-239.**

7. Bryan, D. L.; Mikuriya, Y.; Hempel, J. **C.;** Mellinger, D.; Hashim, M.; Pasternack, R. F. *Inorg. Chem.*, **1987**, *26*, 4180.

8. Carney, M. J.; Lesniak, J. **S.;** Likar, M. D.; Pladziewicz, J. R. *J. Am. Chem. Soc.* **1984,106,2565.**

9. Chen, J. M. Sc. thesis. University of Maine, **1999.**

10. Chen, J.; Jiang, T.; Wei, G.; Mohamed, **A. A.;** Homrighausen, C.; Bauer, J. **A.,** Bruce, **A.** E.; Bruce, M. R. M. *J. Am. Chem. Soc.* **1999,121,9225-9226.**

11. Coffer, M. T.; Shaw, C. F., 111; Horman, **A.** L.; Mirabelli, C. K.; Crook, **S.** T. *J. Inorg. Biochem.*, **1987**, *30*, 177.

12. Connelly, N. G.; Geiger, **W.** E. *Chem. Soc. Rev.* **1996, 96, 877.**

13. Dash, K. C.; Schmidbaur, H. in *Metal Ions in Biological Systems*, Sigel, H., Ed., Chapter **6, 1982, 179-205.**

14. Devenish, R. W.; Goulding, T.; Heaton, B. T.; Whyman, R.; *J. Chem. Soc., Dalton Trans.*, **1996, 673.**

15. Dilorenzo, M.; Ganesh, **S.;** Tadayon, L.; Bruce, M. R. M.; Bruce, **A.** E., *Metal-Based Drugs*, 1999, *6*, 247.

16. Dyson, P. J.; Mingos, D. M. P. in *Gold: Progress in Chemistry, Biochemistry, and Technology.* Schmidbaur, H., Ed., John Wiley & Sons, **1999,** p 511.

17. Foley, J. B.; Bruce, **A.** E.; Bruce, M. R. M. *J. Am. Chem. Soc.*, **1995, 227,9596.**

18. Foley, J. B.; Gay, **S.** E.; Tunnel, C.; Wei, C.; Wei, G.; Jiang, T.; Narayanaswamy, R.; Foxman, B. M.; Vela, M. J.; Bruce, **A.** E.; Bruce, M. R. M. *Metal-Based Drugs*, **1999, 6,255.**

19. Fricker, **S.** P. *Trans. Met. Chem.*, **1996,** *21*, **377-383.**

20. Fricker, **S.** P. *Gold Bull.*, **1996,** *29*, **53-60.**

21. Gusev, **O.** V.; Sergeev, **S.;** Saez, I. M.; Maitlis, P. M. *Organometallics,* **1994, 23, 2059.**

22. Higby, G. J. *Gold Bull.*, **1982,** *15*, **130-140.**

23. Isab, **A. A.;** Sadler, P. J. *Biochim. Biophys. Acta,* **1977,492, 322-330.**

24. Jiang, T. *Electrochemical Studies of Gold(I) Phosphine Complexes,* University of Maine, M. Sc. Thesis, **1991.**

25. Jiang, T.; Wei, G.; Turmel, C.; Bruce, **A.** E.; Bruce, M. R. M. *Metal-Based Drugs,* **1994,** *1*, 419-431.

26. Jones, W. B.; Yuan, J.; Narayanaswamy, R.; Young, M. **A.;** Elder, R. C.; Bruce, **A.** E.; Bruce M. R. M. *Inorg. Chem.*, **1995,** *34*, **1996.**

27. Kamel, H.; Brown, D. H.; Ottaway, J. M.; Simth, W. *Analyst* (London), **1977,** *102*, **645.**

28. Kean, W. F.; Hart, L.; Buchanan, W. W. *British J. Rheum.,* **1997,** *36*, 560-572.

29. Kean, W. F.; Lock, C. J. L.; Howard-lock, H. *Inflammo Pharmacology,* **1991,** 1, **103-114.**

30. Marx, J. *The Magic of Gold*; Doubleday and Company, Inc.: Garden City, NY, **1978.**

31. Mohamed, **A. A.;** Bruce, **A.** E.; Bruce, M. R. M. *Metal-Based Drugs,* **1999, 6, 233-238.**

32. Mohamed, **A. A.;** Bruce, **A.** E.;Bruce, M. R. M. *Organic Derivatives of Gold and silver,* Patai, **S.,** Ed., John Wiley & Sons, chapter **9, 1999, 313-352.**

33. Mohamed, A. **A.;** Bruce, A. E.; Bruce, M. R. M. unpublished data.

34. Morrell, W. P. *The Gold Rushes;* Macmillan: New York, **1941.**

35. Morteani, **G.** in *Gold: Progress in Chemistry, Biochemistry, and Technology.* Schmidbaur, H., Ed., John Wiley & Sons, **1999, p** 41.

36. Narayanasaswamy, R.; Young, M. A.; Parkhurst, E.; Ouellette, M.; Kerr, M. E.; Ho. D.; Elder, R. **C.;** Bruce, A. E.; Bruce, M. R. M. *Inorg. Chem.,* **1993,** *32,* **2506-25 17.**

37. Parish, R. V. *Interdisciplinary Science Reviews,* **1992, 17, 221.**

38. Parish, R. V.; Cottrill, **S.** M. *Gold Bull.,* **1987,** *20,* **3.**

39. Pyykko, P.; Declaus, P. J., *Acc. Chem. Res.,* **1979, 12,276.**

40. Reger, D. L.; Klaeren, **S. A.;** Babin, J. E.; Adams, R. D. *Organornetallics,* **1988, 7,** 181.

41. Ryan, **O.** B.; Tilset, M. *J. Am. Chem. Soc.* **1991,113,9554.**

42. Sadler, P. J., *J. Inorg. Biochem.,* **1995,** *54,* 225-228.

43. Sadler, P. J. *Structure. Bonding,* 1976, *29,* **171-219.**

44. Sadler, P. **J.;** Ni Dhubhghaill, **O.** M. in *Metal Complexes in Cancer Chemotherapy,* Keppler, B. K., Ed., VCH, Weinheim, New York, **1993,222-248.**

45. Sadler, P. J.; Nasr, **M.;** Narayanan, V. L. in *Platinum Coordination Complexes in Cancer Chemotherapy,* Hacker, M. P.; Douple, E. B.; krakoff, I. H. Ed., Martinus Nijhoff, Boston, **1984,** p **290.**

46. Schuhmann, D.; Kubicha-Muranyi, M.; Mirtcheva, J.; Gunther, J.; Kind, P.; Gleichmann, E. *J. Immunol.,* **1990, 145,213**

47. Schwerdtfeger, P.; Bruce, **A.** E.; Bruce, M. R. M. *J. Am. Chem. Soc.,* **1998, 120, 6587.**

48. Shaw, C. F., III in *Gold: Progress in Chemistry, Biochemistry, and Technology.* Schmidbaur, H. Ed., John Wiley & Sons, **1999,260.**

49. Shaw, C. F., III *Inorg. Prosp. Biol. Med.,* **1979,** *2,* 278-355.

50. Shaw, C. F., III *Comment Inorg. Chem.,* **1989**, *8*, 233-267.

51. Shaw, C. **F.,** III; Cancro, M. P.; Witkiewicz, P. L.; Eldridge, P. L. *Inorg. Chem.*, **1980, 19, 3198-3201.**

52. Takahashi, K.; Griem, P.; Goneaiez, J.; Gleichmann, E. *Metal-Based Drugs,* **1994,** *1*, **483.**

53. Tepperman, K.; Elder, R. *Metal-Based Drugs,* **1994, 1,433-444.**

54. Van der Velden, J. W. **A.;** Beurskens, P. T.; Bour, J. J.; Bosman, W.P.; Noordik, J. H.; Kolenbrander, M.; Buskes, J. **A.** K. M. *Inorg. Chem.,* **1984**, *23*, **142.**

55. Van der Velden, J. W. **A.;** Bour, **J.** J.; Stwggerda, J. J.; Beurskens, P. T.; Roseboom, M.; Noordik, J. H., *Inorg. Chem.,* **1982,** *21*, 4321.

56. Van der Velden, J. W. **A.;** Bour, J. J. ; Vollenbroek, F. **A. ;** Beurskens, P. T. ; Smits, J. M. M. *J. Chem. Soc., Chem. Commun.,* **1979,1162.**

57. Vollenborek, F. **A.;** Bosman, W. P.; Bour, J. J.; Noordik, J. H.; Beurskens, P. T. *J. Chem. Soc., Chem. Commun.,* **1979,387.**

58. Vollenbroek, F. **A.;** Bouten, D. C. P.; Trooster, J. M.; Van der Berg, **J.** P.; Bour, J. J. *Inorg. Chem.,* **1978**, *17*, 1345.

59. Wei, **G.** M. **S.** Thesis. University of Maine, **1994.**

60. Witkiewicz, **P. L.;** Shaw, **C.** F., 111, *J. Chem..Soc. Chem. Commun.,* **1981,** 1111-11**14.**

61. Xiao, J.; Shaw, C. F., 111. *Inorg. Chem.* **1992,** *31*, **3707.**

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